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BRITISH MEDICAL JOURNAL

LONDON SATURDAY NOVEMBER 1 1952

TREATMENT OF TUBERCULOSIS OF THE URINARY TRACT*

BY

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Urinary tuberculosis is a focal manifestation of a general disease, and thus treatment must be both general and local. In sanatorium patients suffering from phthisis or bone and joint tuberculosis a symptomless bacilluria is not uncommon: it necessitates a complete urological investigation, but in many cases no lesion can be demonstrated. Medlar (1926) and Band (1942), after prolonged study of this subclinical form of urinary tuberculosis, found that both kidneys contained microscopic tuberculous foci and that such foci often healed. It is thus a cardinal rule that there is no place for surgery unless a lesion can be demonstrated by pyelography or by *x*-ray or cystoscopic examination.

It hardly seems necessary to say that the most common initial symptom of urinary tuberculosis is increased frequency of micturition. This symptom, associated with pyuria and an absence of pyogenic organisms, should be regarded as probably of tuberculous origin, apart from that uncommon disease abacterial pyuria. Demonstration of the tubercle bacillus is necessary, and if this is not possible on the examination of a single specimen of urine the search should be continued from several 24-hour specimens. Culture and guinea-pig inoculation must also prove negative before this infection can be excluded. A symptomless pyuria found by chance, as during a life assurance examination, is not uncommonly due to renal tuberculosis where the lesion is shut off intermittently by calcification in the ureter. The following case illustrates this.

A man aged 31, enjoying perfect health and employed as a tea planter in India, decided to take out a policy of life assurance. At the examination slight pyuria was discovered and tubercle bacilli were found. He returned to this country for nephro-ureterectomy, as pyelography had demonstrated a functionless right kidney and a normal left kidney. On arrival here repeated examination of 24-hour specimens of urine, culture, and guinea-pig inoculation was negative: the urine was normal and there was no pus or blood cells. Cystoscopy showed an indrawing of the right ureter mouth, into which a catheter could be inserted only for a distance of 0.5 cm., but an otherwise normal bladder. *X*-ray examination showed a few calcified areas in the kidney and considerable calcification in the ureter below the right sacro-iliac joint. Otherwise the findings of the Indian surgeon were confirmed. Nephro-ureterectomy was performed and the kidney found to be grossly affected by caseo-cavernous lesions, and tubercles were visible throughout the cortex.

This case illustrates the importance of repeated urine examination when pyuria is present and, in certain cases, the element of luck in diagnosis when the pyuria is intermittent.

As I have previously stated, urinary tuberculosis is a focal manifestation of a generalized infection—it is always secondary to another lesion elsewhere which may be latent. Investigation and treatment thus must be both general and local.

General Treatment

General treatment demands a sanatorium régime, which may include treatment by streptomycin and *para*-aminosalicylic acid (P.A.S.); but whether this general treatment is carried out in a sanatorium or not must be left to the discretion of the medical attendant. The effect of streptomycin and P.A.S. on urinary tuberculosis has been investigated on behalf of the Medical Research Council by Jacobs and Borthwick (1950) and Jacobs (1951), and they seem to have proved that no known chemotherapeutic agents or antibiotics, alone or in combination, can be depended upon to cure or control an established renal focus. These substances must therefore be regarded as an adjunct to other forms of treatment, and meantime the best therapy is prolonged sanatorium care and the extirpation by surgery, where possible, of any demonstrable focus. Jacobs (1952) states that from chemotherapy the following benefits may be expected: (1) *A tubercle-positive urine can be rendered tubercle-negative*, but in the presence of a renal focus of more than microscopic dimensions this change is likely to be transient. (2) *Mild secondary cystitis and superficial bladder ulceration generally respond to the treatment with a corresponding improvement in the symptoms.* These benefits are chiefly observed in those suffering from clinical unilateral renal lesions on whom nephrectomy has been performed. (3) *As an "umbrella" for nephrectomy, partial nephrectomy, or epididymectomy* streptomycin is probably a safeguard in preventing haematogenous dissemination and sinus formation.

Treatment by these and other antibiotics, and by chemotherapeutic agents such as the thiosemicarbazone

*Paper read in opening a discussion at the Medical Society of London, on April 28, 1952.

drugs (Cosbie Ross, 1951) and *iso*nicotinic acid hydrazide (*British Medical Journal*, 1952; *Lancet*, 1952), is being evolved rapidly, but meantime it consists as a rule in the administration of streptomycin in doses of 0.5 g. morning and night to a total dose of 40 g. P.A.S. is also recommended to be given simultaneously, as it appears to increase the effect of the streptomycin and lessen the chance of the bacilli becoming resistant. For an adult 20 g. daily is given in divided doses four times a day over a period of six months or longer, the duration of the treatment being influenced by the response.

Because of the increased tendency to cicatrization associated with streptomycin therapy, sequelae of a character which worsens the condition of the patient may result. It therefore is not permissible to give the treatment indiscriminately with the idea that should no benefit be obtained no harm will result. According to Jacobs (1952), the drug should be withheld in the following circumstances: (1) *Urinary tuberculosis associated with advanced bilateral renal lesions or an advanced lesion in a solitary kidney:* no benefit can be expected from the treatment, and the risk of toxic symptoms is therefore not worth taking. (2) *A severe constriction at the uretero-vesical junction or a well-marked stricture of the ureter, particularly when associated with a single kidney:* the increased cicatrization resulting from streptomycin may be followed by hydroureter and hydronephrosis. (3) *Severe secondary cystitis associated with marked bladder contracture:* the contracture already present may be worsened as a result of the increasing cicatrization caused by streptomycin.

Surgical Treatment

If surgery is decided upon, the operation should be performed when the peak of general condition and power of resistance is attained. The timing of that peak should be determined by an experienced tuberculosis physician. In a patient suffering from renal tuberculosis whose general condition is satisfactory the minimal period of preparation for operation should be two weeks, during which he should have treatment with streptomycin and P.A.S. while resting in bed.

Operative treatment will naturally depend on the site and extent of the lesion. The treatment which has been found most suitable for the various types of lesion is as follows:

1. *Where there is any demonstrable renal lesion with or without cystitis* nephrectomy is indicated. On exposing the kidney at operation the upper ureter should be palpated, and where disease, denoted by enlargement and thickening, is found that ureter in its whole length should be removed with the kidney. Thus the operation in these cases is not nephrectomy but a nephro-ureterectomy. A common complication following nephrectomy alone for renal tuberculosis is the formation of a chronic sinus. This is unknown in my unit, where for over 20 years the practice has been nephro-ureterectomy *en bloc* except where the ureter appears normal: in such cases we are content with the removal of the upper 4 in. (10 cm.). A short description of the technique might be of interest.

The kidney is exposed through an oblique incision in the loin, and by gentle finger or scissor dissection it is freed and, if possible, partially exteriorized. The vascular pedicle is then carefully exposed by dissection, double clamped, divided, and trebly ligated. The ureter is examined, and if it shows the least abnormality it is freed down to the level of the iliac vessels. The incision is now closed except for the small opening through which the ureter issues with its attached kidney hanging free. The patient is rolled on to his back and a vertical incision made in the midline. The peritoneum is exposed and retracted inwards and the ureter easily identified by gentle traction on the kidney; it is dissected and freed to the bladder wall, at which point it is divided between clamps by a scalpel the blade of which has been dipped in pure carbolic acid solution. Both ends of the divided ureter are then separately treated by carbolic acid followed by spirit, doubly ligated, and the clamps removed. The end of the ureter attached to the kidney is inserted into a sterile finger-stall, which is then tied over it, and, following on that, the kidney is pulled on and removed complete with its ureter. Both wounds are now completely closed without drainage, and healing is by first intention. The extra time required to remove the ureter with the kidney is about ten minutes, and the resulting added strain on the patient is negligible. By this radical operation continual seepage of tubercle bacilli into the bladder is obviated and ulceration prevented, or, if already present, given a better chance to heal.

2. *Where the lesion found on pyelography is a small ulcero-cavernous lesion affecting a polar calix of one kidney* the treatment of choice is partial nephrectomy. The indications for this operation are uncommon, and I have found only one case in which I thought it justifiable; the result after two years is satisfactory and the urine remains tubercle-negative. The method undoubtedly has a place, but the selection of the case requires experience and judgment, and the operation calls for great technical ability. In an unsuitable case it is a hazardous procedure, with the possibility of a later and difficult nephrectomy performed on a patient in poor condition.

3. *Where both kidneys show demonstrable renal lesions* operation, generally speaking, is contraindicated. Treatment in a sanatorium combined with streptomycin and P.A.S. offers the best chance. The progress of the disease should be checked at intervals by pyelography. If one kidney is grossly diseased and the other shows only a minor lesion nephrectomy or nephro-ureterectomy of the severely affected organ may prevent spread of the disease in the less-affected kidney and in the bladder. If the lesion in the better kidney is minimal and stationary a partial nephrectomy should be considered at an interval after removal of the worse kidney.

4. *Where one kidney has already been removed and the remaining kidney is affected* the possibility of operative extirpation of the disease will depend on whether the focus is confined to one pole of the kidney. In a few cases partial nephrectomy may be possible.

5. *When the patient has an active lung lesion in addition to a renal lesion* the operative treatment of the renal lesion must await control of the more serious lesion before surgery is attempted. The lung lesion spreads more rapidly and is a greater danger to life than the renal lesion, and thus in these cases the surgeon must be guided by the tuberculosis physician.

Tuberculous Cystitis

The treatment of tuberculous cystitis, apart from the extirpation of gross foci in the kidney and ureter, actually depends on the size and depth of the bladder lesion. In most cases removal of the affected kidney and ureter leads to healing of the bladder and relief from symptoms. This process is gradual and may take several months. It can be accelerated by a sanatorium regime. Where the tuberculous ulceration is superficial the administration of streptomycin and P.A.S. encourages more rapid healing. When the ulceration is deep, however, interstitial changes develop in the bladder wall; these drugs should then be withheld owing to the increased fibrous contracture they are likely to cause. Where this interstitial fibrosis has in fact occurred the change is irreversible, and the bladder, incapable of distension, can contain at most only a very small quantity of

urine. Frequency becomes acute and may ultimately reach virtual incontinence. The ureters are affected by back pressure arising from the contracted bladder or fibrosis and stricture of their lower ends, and hydroureter and hydronephrosis result. Renal impairment becomes progressive, with ultimate death from uraemia.

The only way to save a patient so affected is to divert the urinary stream from the bladder to the colon or skin, and this should be done before hydronephrosis is established. Bilateral renal involvement with tuberculosis or the presence of a solitary diseased kidney is not necessarily a contra-indication. The urinary diversion may not save life, but it will certainly prolong it and ensure some measure of comfort. Transplantation of the ureter or ureters into the colon is now a well-tried procedure and gives the minimum of discomfort and after-trouble, but in a very occasional case it may be preferable to bring the end of the ureter to the skin surface. The difficulty here is the collection of the exuding urine without leakage with all its discomforts. In such a case the formation of a skin-covered spout, or nipple ureterostomy as described by Band (1950), makes leakage unlikely and may add greatly to the patient's comfort and well-being.

Epididymectomy

Tuberculosis affecting the epididymides, the seminal vesicles, and the prostate can result from a direct blood spread, but often it follows infection of the prostate direct from the prostatic urethra. Although this paper concerns urinary tuberculosis, it must be remembered that at least 50% of cases of genital tuberculosis result from a renal source by direct spread through the ureter, bladder, posterior urethra, prostate, and seminal vesicles to the epididymides. Hence it follows that in any case of chronic epididymitis a complete investigation of the urinary tract is necessary. When a focus is found in the kidney, nephrectomy, and possibly ureterectomy, followed by sanatorium treatment, may be enough to arrest the disease, but in some cases epididymectomy will be required in addition.

Conclusion

Might I summarize by again repeating that tuberculosis of the urinary tract is a focal manifestation of a generalized infection, and thus investigation and treatment must not be confined to one system. The principles of treatment are by rest in suitable environment, adequate nutrition, and the aiding of the body's defences by suitable antibiotics and chemotherapeutic measures. When the local lesion is demonstrable general measures are never enough and surgical extirpation is essential, but it must be undertaken only when the patient has reached the optimum condition likely to be achieved by a sanatorium régime, and it must be followed by the prolonged rest and treatment required to ensure against recurrence of active disease. Finally, it cannot too often be reiterated that surgery alone is not enough; it can only be regarded as one of the weapons in the attack on this major killing disease.

I desire to express my thanks to my friends and colleagues, Mr. D. Band, Mr. W. M. Borthwick, and Mr. A. Jacobs, who have been pioneers in the modern investigation and treatment of genito-urinary tuberculosis, for their willing help and permission to quote from their experience.

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CLINICAL PSYCHOLOGY AND SOME FORGOTTEN EPISODES*

BY

The Late MILLAIS CULPIN, M.D., F.R.C.S.

One-time Professor of Medical Industrial Psychology, London School of Hygiene and Tropical Medicine, and Lecturer on Psychoneuroses at the London Hospital Medical College

We can all talk about psychology now, though when I qualified 50 years ago one rarely heard the word. Since then I have been carried along on a stream of events related to clinical psychology and with a curious repetitive pattern. These I propose to recapitulate, with the intention of drawing a moral from them.

The Hysterical Symptom in Wartime

The stream caught me when in November, 1914, I joined the R.A.M.C. and became the surgical member of a board in London for sick and wounded officers. At that time the war neuroses had not been recognized and shell-shock was not yet invented. Many of the officers we boarded suffered from functional troubles, chiefly hysteria, and brought to us diagnoses of physical disorders that for me did not exist. I was taken aback, for I could not believe I was a better diagnostician than the élite of Harley Street. I am less diffident now, but I did not realize then that to make a correct diagnosis—in one case or many—would set up the insoluble problem of what to do next. Nobody likes insoluble problems, and my attempts to draw official notice to what was happpening did not meet with encouragement. In the new year I was transferred to the Alexandra Hospital, near Portsmouth, as a surgical specialist, but before that, having seen how frost-bite (later called trench-foot) was carrying a heavy load of hysteria, I joined my old colleague E. G. Fearnsides in examining a batch of men in hospital with that diagnosis, and we published a paper in 1915 declaring that many of them showed hysterical symptoms. So far as I know this was the first mention of war neuroses in our literature.

At the Alexandra Hospital, if I made the diagnosis of hysteria I had to face for myself the problem of what to do next. Thus when I insisted that a man in my ward, supposed to have tuberculous disease of the tarsus, really presented a hysterical clubfoot, for which I could do nothing, I was assured that the War Office would not accept the diagnosis of hysteria as an invaliding disability and I must board him out as a sufferer from tuberculous disease. I cannot detail the manœuvres that led to his being invalided out with the correct diagnosis, but within a few weeks he had re-enlisted and his new M.O. wrote to us asking what had been his disability. Soon after this, when a similar case appeared before an invaliding board as talipes varus following osteoarthritis, and I demurred at putting my name to that diagnosis, the man was sent to my ward to be dealt with as best I could. After a time the M.O.s of neighbouring units sent their tricky cases " for surgical opinion and advice." I found myself carrying on an out-patient clinic and sometimes obtained satisfactory results by common-sense methods —methods made up of persuasion and exhortation aided

*This paper is based upon a B.M.A. Lecture given to the Norfolk Branch of the British Medical Association on April 9.

by a certainty of surgical diagnosis and the confidence born of psychological ignorance. In 1916 I published an article on practical hints on functional disorders, and the following case, there described, shows how I had reached a dangerous facility in removing the presenting symptom of a severe psychoneurosis:

An officer was wounded in the right arm; the musculo-spiral nerve was said to have been sutured, and he was treated by massage and electricity for seven months (for this I was partly responsible). His hand and forearm were then as if carved from wood, without movement and anaesthetic. He was to appear before a medical board in a fortnight, and feared being invalided out of the Service. His condition was at last recognized, a straight talk followed, and the board passed him as fit for general service, his musculo-spiral nerve being found to function perfectly.

He wrote me a grateful letter from France, but I read the rest of his story in a daily paper. He was invalided home bedridden from paralysis, and, after a visit from a specialist, made his way to another room, found his revolver, and shot himself. A retrospect brought up some traits—overscrupulousness, hesitancy of speech, peculiar tics—suggesting pathological doubts and fears that finally defeated him.

Shell-shock

Service in France kept me busied with gas gangrene and such-like, but I became acquainted with shell-shock and was able to note the change-over of opinion about it. How many of you know that its victims appeared in the casualty lists as "wounded, shell-shock," and wore decorative wound-stripes to indicate that they had suffered by enemy action? It was assumed that the trouble was due to physical disturbance of the central nervous system, and the literature of the period gives us theories about separated synapses, dissociated cerebral centres, carbon monoxide poisoning, and what not; and on the German side a similar assumption was made. But here was a mass epidemic that, unlike the individual cases of hysteria, could not be ignored; the war might have come to an untimely end if, on both sides of no-man's-land, the soldier who had reached his limit of emotional endurance could be hurried home and greeted as a wounded hero. So the official use of the phrase shell-shock was prohibited, and instead of the wounded-hero tune we heard, "Shell-shock? I'd soon cure shell-shock. I'd shoot every man that had it." This met the need for the speaker to express moral indignation about what he couldn't understand.

Towards the end of 1917 I came home on leave, and whilst airing my views met the late Colonel Aldren Turner, then in charge of what we should call Army psychiatry. Taking me seriously, he said the Army had more surgeons than it needed but he could not find men to look after his people. Would I drop surgery for a time and help him? If so, he would send me to Maghull for three months' training, for the war had revealed some lamentable defects in our medical education, and perhaps mine was not perfect. Curiosity sent me to Maghull, and I soon had to admit the existence of much clinical material about which I had been taught nothing. This was apart from modern theory, which cleared up some of my problems and offered methods of treatment conforming to the basic dogma that two and two must make four.

D.A.H.

Now followed a long spell in neurological hospitals. There my men told me about their faintings and palpitations and shortness of breath, and I noted their blue hands and pulses up to 150 or so. I rarely examined a heart, but would tell a man his nervousness was making his heart go all floppy, and when we had dealt with the nervousness the heart would come all right. I did not say there was nothing the matter with the heart, and so far as my memory goes the men accepted my explanation. One evening, in an idle moment, I picked up an article on disordered action of the heart and received another shock. This was what half my men suffered from and I hadn't known it. Only as time went on could I believe that it was pure chance whether a man was sent to my hospital as a neurotic (I have to use that word, though I dislike its mixed flavouring of mythopathology and moral judgment) or to a heart hospital as suffering from D.A.H.

Of this latter condition Sir James Mackenzie (1925) wrote: "Hospitals for the investigation of the heart were set apart; groups of doctors with special knowledge were detailed for this investigation, and every conceivable device was employed. For several years such investigations were pursued with the greatest industry, and if to-day we seek for the increased knowledge of the heart that has accrued it will not be possible to detect the slightest gain."

After some experience on pension boards I wrote an article (1920b) that ended: "But the majority of cases found among pensioners and diagnosed D.A.H. are entirely of psychogenetic origin. If this fact could be generally recognized it would aid in the restoration to social usefulness of some of the men who now regard themselves as permanent invalids."

In the recent war D.A.H. was bound to recur. There was general agreement to call it "effort syndrome," and after some rearguard skirmishing it was made a responsibility of the psychiatrist. Its numerical incidence was very low by comparison with that in the earlier war.

Railway Spine and Traumatic Neurasthenia

So far shell-shock and D.A.H. stood by themselves as mass diagnostic errors, but after I published (1920a) my M.D. thesis on the war neuroses I received a letter from Herbert Page, written with a noticeable tremor, saying he had read my book, that all the symptoms of shell-shock would be found in his book, *Railway Injuries* (Page, 1891), but the lesson he had tried to teach had been forgotten. His book had to do with Erichsen's "railway spine," a condition still mentioned in my student days but attributed to traumatic neurasthenia. Erichsen (1877) had described at great length symptoms that I have seen only in a ward full of titubating shell-shockers, and he invented theories of concussion of the spine, meningeal irritation, ascending or descending degeneration, meningomyelitis, and such-like. His position made his views authoritative, and it took years of controversy to destroy this fancied pathology, which was, however, buried so obscurely that but for Herbert Page I should never have known about it. I had the privilege of meeting Page, and in our talk about railway spine I mentioned psychology. He shook his head. "I don't know anything about psychology," said he; "I only knew it was something the matter with the man himself."

Traumatic neurasthenia was a diagnostic stand-by for years after railway spine was blown upon, but Sir Farquhar Buzzard (1923) attacked the idea that "an injury of any degree of severity and inflicted at any site may produce a physical condition of the nervous system, with characteristic signs, but without any morbid anatomy, to which the name traumatic neurasthenia is fairly applicable." I once examined in a Midland town 10 miners receiving compensation for the disorder, and wrote up the experience (Culpin, 1931), for each case was a museum specimen. One man, for example, received an injury to his back in 1925, and I was shown a sheaf of reports about his back and his nerves. At the interview with me he complained that he was not feeling well. "My back gives way when I walk. I burst into a sweat if I slip. I get pain in the head on bending. The strength goes out of my legs. I can't stand the noise of picture shows. I get a pain in the privates." I asked, "Do you feel anything else the matter?" and pressed the

question without eliciting further symptoms. His wife was there, and I asked her, "How does he sleep?" She told of how she wakes him up because he makes all sorts of noises. The man, asked about these noises, now said: "I dream of the accident, and the wife wakes me up," then admitted that he was restless and afraid in a room by himself (claustrophobia), was frightened in the dark. "If I meet a cat or dog in the night I burst out all of a sweat. I'm nervous in a bus. On the pavement I keep thinking the buses are running into me." Asked whether he could go down the pit if his back were all right he said, shamefacedly but sincerely, "It's not a nice place to go when you are frightened." A recognition of this man's disability might have saved years of waiting for him to go down the pit again.

I recorded in 1943 how the failure to value properly the importance of neurotic symptoms in relation to coal-mining sent three "Bevin boys" to prison. In one case the secretary of a miners' lodge said the lad was pit-nervous and it was unsafe for him to go down the pit. "Pit-nervous" is good.

Traumatic neurasthenia has faded away. I regret that anxiety neurosis, which once had a meaning, has so far taken its place that my evening paper lately reported Mr. Justice X as causing loud laughter in court when he said, "The typical cause of anxiety neurosis is the anxiety of the plaintiff who wishes to recover damages."

Night-blindness as an Epidemic Artifact

I have described (Culpin, 1933) hysterical night-blindness in connexion with miners' nystagmus, and as an extensive epidemic in the Continental armies during the 1914–18 war. Alarmed at possibilities here, I wrote (Culpin, 1940) a warning that if we talked enough about vitamins and night-blindness we might start an epidemic. "Then," said I, "psychopathologists will declare the nature of the disorder and will be derided at first; but when the epidemic is well established and the cases are thoroughly ripened they will be called upon to treat it."

It all came true. In 1941 our newspapers carried pictorial advertisements showing how the nocturnal streets looked to the victims of night-blindness, and telling them what to cure it with. Radio comedians made gags about it, vitamin fans ate carrots till their skin turned yellow, and at least one scientific-looking article, full of graphs and what-not, treated the disorder as if it were a result of eating food deficient in vitamins. Then Dr. E. Wittkower and his team (1941) in Glasgow, examining some 50-odd soldiers with this epidemic night-blindness, found it was only an excrescence upon deeper troubles and that "most of them, quite apart from their night-blindness, were unfit for military service because of their psychological abnormalities and disorders." Dr. F. M. R. Walshe (1941), taking his share in the fulfilment of prophecy, was delightfully derisive of this work. Then an official circular was sent to Army ophthalmologists telling them that for practical purposes night-blindness did not exist in the absence of gross ocular disease and any difficult cases should be referred to a psychiatrist. To my prophecy I should have added that the affair would be forgotten as soon as possible and some people would deny that it had ever occurred.

Unconsciousness and Deep-diving

Such episodes as these do not arise through lack of knowledge. Was not Erichsen a president of the Royal College of Surgeons? They are due to a wrong but rarely questioned philosophic outlook which at this time of writing I can only declare to exist. Behind it is a long history, which I have set forth (Culpin, 1945).

This outlook is manifest in almost any issue of any of our professional journals, but an attempt to discuss a specific example might appear as a personal attack upon a writer. In one example, however, in which I was concerned, the same problem was tackled by opposite methods, dependent upon what may, for the time being, be called respectively the animistic and the mechanistic outlook, and both methods are on record with their results. The animistic outlook is still so unfamiliar that I must give the whole record from the original publication (Culpin, 1933) (permission to quote this has kindly been granted by the honorary editors of the *Proceedings of the Royal Society of Medicine*):

"To increase the depth at which divers work, Sir Leonard Hill has invented a decompression chamber which the man enters on his way to the surface,* his helmet is removed and he receives refreshment, whilst the chamber is sealed and hoisted on deck, where decompression can be carried out at leisure, thus avoiding the danger of caisson disease. By this means a depth of 300 ft. can be reached with safety. But unexpected things happened; some men carried out the deep diving successfully, others sent up erratic signals by telephone or lifeline and on return to the surface claimed to have been unconscious. One man to whom that had happened demanded to be pulled up on another occasion before he reached his depth, and declared that he had seen his own face looking at him through the window of the helmet.

"Physiological theory could not account for these happenings and the Medical Research Council, when approached about the problem, suggested a psychological attack upon it. I was asked to undertake this and, with the assistance of Surgeon Lieutenant-Commander Phillips, I examined half a dozen divers, of whom two had suffered this unconsciousness.

"From the first of these two, a well-built healthy Petty Officer, I elicited the following symptoms: Always nervous of doing the wrong thing, even when being dressed for diving. 'I don't like to attract attention in the street.' Would not go into a strange tea-shop alone, would feel that everyone is watching him. Would rather go hungry. Never afraid of the dark, but of closed spaces—feels sealed in. The terror (his own word) came on first when skylarking, when other chaps fell upon him.

"Plays football and hockey. Useless in the water. 'I don't like it.' Would bathe in the sea but not go out of his depth. Yet has passed his swimming tests.

"Did quite well at ordinary diving; fear of being closed in came on badly once but passed away. 'It came on that time just before I went off on the bottom. That stirred it up and I've had it off and on since.'

"Describing his dive, he said: 'I felt dizzy at 40 (fathoms); at 45 felt in a nightmare. Felt like going under ether—that made me think of going unconscious. I had the feeling of closed in, and went off. When I came to daylight I came to my senses,'—i.e., about 100 ft.

"Then he described his second attempt, when he experienced various hallucinations and had to be pulled up. I now put him on a couch and directed him to go over the first descent and talk of it as if it were happening now. With some urging on my part he repeated the performance and recalled with hallucinatory vividness what seemed to be the whole of the period for which he had claimed unconsciousness. He cried out, 'Pull me up, for God's sake pull me up'; 'I feel as if I'd never go up'; 'I'm tied on the bottom. My mouthpiece is caught under my nose. It's getting lighter now. I can see the chamber.'

"The case is clear. The man was a claustrophobe and his 'unconsciousness' was a state of *Angst*.

"The second man, an engine-room artificer, provided less striking symptoms. He has the feeling of being watched, but has got over the tea-shop fear. He takes measurements two or three times at his work; says, 'There's always the possibility of trouble.' Was afraid of the dark but has got over it. Not keen on being in a crowd (a mild phobia). Has good days and bad days. 'If things have been going wrong, I wonder what's going wrong next.'

"He described one descent: 'All right till I touched fifty fathoms. Thought I was all right. Did my job. Didn't feel very bright. Was proud of myself. Was about to look round at the light and knew nothing more. They say I gave correct signals.'

"Like the other man, on a second attempt he demanded to be pulled up.

"I postponed the attack upon his amnesia till I secured the presence of my colleague, Dr. A. E. Phillips, when I asked him

*Out of respect to the memory of Sir Leonard I must record that he reproved me for carelessly attributing this invention to him instead of, if I remember aright, to Sir Robert Davis, of Siebe, Gorman and Co.

to take down everything I said and everything the man said.* Using the same technique as before, I induced a hypnoidal state in which he recapitulated the whole episode with minute detail and appropriate actions but little emotion. The verbatim account occupies 1¾ foolscap pages, and I only spoke 41 words after he began. He reproduced the conversation over the telephone, and, by an extraordinary piece of luck, Dr. Phillips had been at the other end of the telephone during the actual dive and was able to affirm the verbal accuracy of the reproduction. I think that makes the experiment unique.

"So far, then, we could assure the authorities that the manifestations were not due to any defect in their physiological theory or practice—an important matter to them. That physiologists welcomed the psychological explanation is perhaps also unique.

"It was obvious, moreover, that the presence of a minor psychosis could have been recognized beforehand in these two men. This was being wise after the event, but in the following year Dr. Phillips was still in medical charge of men selected for training in deep-diving, and decided to put his psychological experience into practice. He 'vetted' five men and asked me to vet them independently. We both agreed that one of them might readily fall a victim to the occupational neurosis, but for various reasons decided to let him carry on. His most important symptom in my view was a phobia of horses. The result of the dive to 300 ft. is described by Dr. Phillips in a paper given to the United Services Section [18]. The man demanded to be brought up, and emerged from the chamber in a state of collapse. Dr. Phillips decided to make the man abreact the experience and the dramatic result is described in his account:

"'With sweat like a stream of water running down a face the colour of chalk, dilated pupils and rolling eyes, he went through all the emotions of the dive, sobbing and tearing at his clothes under the impression that he was again in his diving-suit, and clawing at his face to pull off the imaginary face-glass. It was a picture of stark mad terror and the impression it left is very difficult to describe. No earthly power could then have got him near a diving-suit.

"'The interview lasted until about 10.30 (from 9.0), and when he had "come to" again there was an immense improvement in his condition. The deep sigh which heralded in the return to external consciousness was indicative of the dam which had been loosened.'

"Such abreaction I regard as essential for the prevention of further symptoms after terrifying experiences. I have described a case [19] in which the effects of a fright during compressed-air work were ascribed to caisson disease and a severe psychoneurosis was allowed to develop which, I believe, a timely abreaction would have prevented."

The other record (Donald, 1947) tells us that "the investigations of oxygen poisoning described here were started in April, 1942, owing to the occurrence of several cases of unconsciousness in oxygen-breathing apparatus at depths and in times that were then considered to be safe." This was a restatement of the problem that had presented itself in 1930, the introduction of oxygen-breathing having made no difference to what happened. A painstaking study of the physical effects of oxygen under all sorts of conditions (time, pressure, exercise, and so on) was carried out. The symptoms, reported at length, included vertigo, nausea, and syncopal and convulsive attacks, a long paragraph being headed, "Toxic Effects of Oxygen on Brain Metabolism." No conclusion, however, was reached about why several cases of unconsciousness occurred at depths and in times then considered safe. I wrote (Culpin, 1947) suggesting that Dr. Kenneth Donald and I had been concerned in the same problem, but no discussion followed.

*Without a witness my account might have been discredited, for this procedure was then under a cloud. Now it is correct and praiseworthy, though as a propitiatory ritual the physician should put on a white coat and inject some thiopentone. Let me explain that the first diver reproduced a story I had heard so often from shell-shockers: "Then I became unconscious and I came to myself when I reached the dressing station"—or the C.C.S., or the base hospital, or wherever there was freedom from fear. This "unconsciousness" had been regarded as due to concussion and became the starting-point of the shell-shock theories, but was really the blotting out of a period of terror the memory of which could be revived by a simple technique. The diver said, "I had the feeling of closed in and went off. When I came to daylight I came to my senses." This gave me the diagnosis, which I confirmed by using the same technique as that used for the shell-shockers.

Conclusion

Common to these episodes is a particular kind of diagnostic failure. Their recurrence through the years suggests that this failure is a constant factor in medicine, and recent discussions about the prescribing of placebos show a lamentable acquiescence in it.

When I lectured to students about the psychoneuroses I found I could get them interested in psychological theory, but I assured them that, as a clinician, my aim was to enable them to elicit a patient's symptoms and recognize their significance. I had to warn them, however, that my stuff was no use for examination purposes and they had better leave it behind when they entered the examination-room.

We shall have made some progress towards remedying our failure when at a qualifying examination it becomes possible for an examiner to expect from a candidate an intelligent response to the request, "Will you please find out what neurotic symptoms that man has and tell me what you make of them?"

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SIGNIFICANCE OF TESTICULAR EXFOLIATION IN MALE INFECUNDITY

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Infecund semen often contains numerous exfoliated testicular cells (Lane-Roberts *et al.*, 1939, 1948; Baker, 1939; Moench, 1940; Joël, 1942; Staemmler, 1942–3; Belonoschkin, 1949; and others). Incidental observations had suggested to us that exfoliation was of diagnostic significance, and special attention was therefore paid during the past six years to such cases. The present communication reviews some data and conclusions which require but simple methods for their verification and which may be of interest to the clinician.

Recognition of Exfoliated Cells

By comparing the cells in semen with biopsy and post-mortem sections most testicular cells can be readily recognized as such, provided stained semen films are examined—for example, wet films stained by the osmic-acid–Giemsa method (Lane-Roberts *et al.*, 1948). The most common cells have a single unfragmented nucleus but differ greatly in size. One type has a cell diameter of 10–15 μ, with a nuclear diameter of 8–12 μ; the chromatin may be concentrated in a skein, the cell having preserved the appearance of the spermatocytes familiar from cross-sections through the seminiferous

tubules (see Figs. 4 and 5). Other cells of this group are less well preserved and may show pyknosis and distortion of the nucleus (Fig. 3). Usually such cells can be identified as exfoliated spermatocytes. The second type of cell, which corresponds to a spermatid, is much smaller (diameter 5–10 μ) and shows less variation except with respect to the position of the nucleus, which is not infrequently found in process of being extruded.

These cells correspond essentially to normal stages in spermatogenesis, though their presence in large numbers indicates that spermatogenesis is abortive, at least in some areas of the epithelium. Of greater biological interest are other types of exfoliated testicular cells—namely, the binuclear and multinuclear cells. The binuclear cells vary greatly in size (6–25 μ) (see Fig. 1, also Lane-Roberts *et al.*, 1939, Fig. 20). In some binuclear cells the nuclei are connected by an isthmus of chromatin as if an "amitotic" division had been arrested. In others the nuclei are separated from each other while the cell body seems to have been arrested in the process of division. Also, small binucleated cells may show partial differentiation, and a series of transitional forms links them with certain duplex forms of spermatozoa—for example, double-headed sperms.

FIG. 1.*—Exfoliated testicular cells in semen. Note (*a*) large binuclear cell (near lower margin), (*b*) small binuclear cell (near left-hand margin), (*c*) large mononuclear cells (near right-hand margin), (*d*) spermatozoa, (*e*) extruded nuclei and nuclear remnants. (Dry film. ×320.)

The multinuclear cells are of varying shape and size (largest diameter 9–28 μ). The number of nuclei varies from three to nine (Figs. 2, 4, and 5). The nuclei may be well preserved, and are distinct from the fragmented nuclei seen in some degenerating epithelial cells. They clearly correspond to the giant cells found in human post-mortem testes (see Oberndorfer, 1931, and other references marked with asterisk) and also in testicular biopsies. Though sometimes mistaken for polymorphs, these cells differ from the latter in being much larger, apart from other distinguishing cytological characteristics.

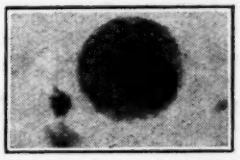

FIG. 3. — Exfoliated testicular cell in semen (large mononuclear cell with pyknotic nucleus). The adjacent spermatozoon (duplex form) lies in a different optical plane. (Wet film. ×920.)

The presence of binuclear cells indicates that exfoliation may not be limited to the interception of a normal process, but may involve the production of abnormal cells. Their structure reflects a disturbance which besets the cell at varying stages of division and arrests the latter. Such "antimitotic" effects probably also account for the occurrence of multinuclear cells; the alternative explanation, invoking fusion of spermatids or spermatozoa (cf. Maximow, 1899; Morgenstern, 1923; Kraus, 1928; Stieve, 1930), does not equally well account for the presence of multinuclear cells in biopsy specimens where spermatogenesis ceases at spermatocyte level.

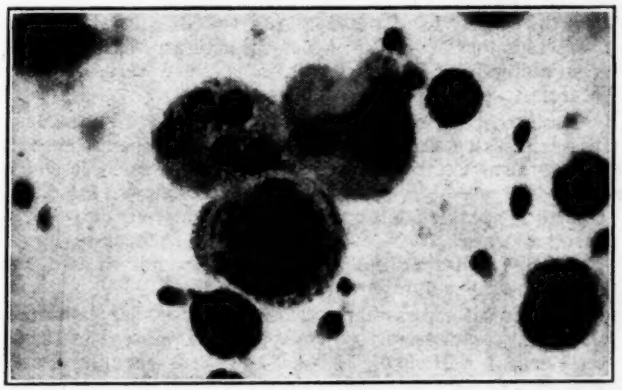

FIG. 4.—Exfoliated testicular cells. Note (*a*) partial preservation of skein in large mononuclear cell; (*b*) large binuclear cell with one pyknotic nucleus; (*c*) multinuclear cell; (*d*) differentiated spermatozoa. (Dry film. ×920.)

FIG. 2.—Exfoliated testicular cells in semen. Note (*a*) small binuclear cells—for example, upper left corner and near centre of upper margin; (*b*) large cell with nucleus in arrested division (near left-hand margin); (*c*) multinuclear cell (centre); (*d*) various types of large mononuclear cells; (*e*) fully differentiated spermatozoa. (Dry film. ×320.)

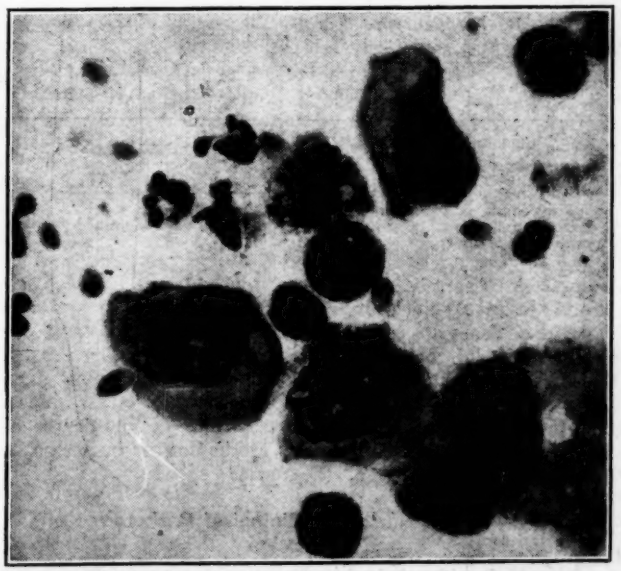

FIG. 5.—Exfoliated testicular cells in semen. Note large mononuclear cells and multinuclear cell (cf. with polymorph near lower margin). (Dry film. ×920.)

*Figs. 1, 2, 3, and 4 were made from a slide of a semen specimen obtained by Dr. H. G. Close. The degree and variety of exfoliation in this specimen rendered it particularly suitable for demonstration.

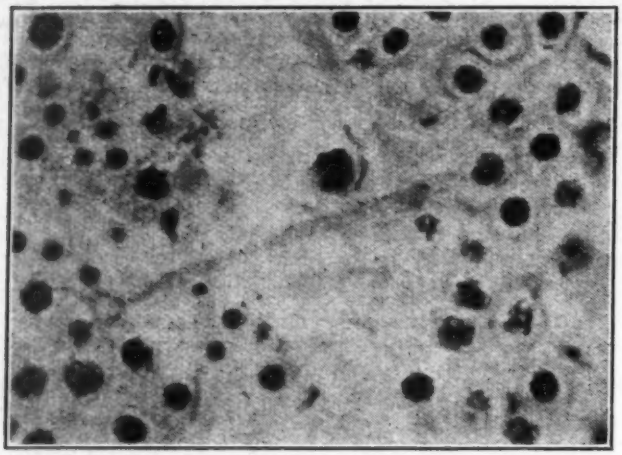

FIG. 6.—Exfoliated multinuclear cell in seminiferous tubule. (Biopsy specimen. ×560.)

Density of Exfoliated Cells

All types of cells may be present in a single specimen of semen; more commonly one or the other type predominates. Small cells with a single nucleus and small binuclear cells are the most common forms. Their density may be estimated directly in a haemocytometer using stained semen, or, more simply, by an indirect count; in the latter the density of spermatozoa is established first by the usual count and then the cells and spermatozoa are counted in a stained film, using a number of fields in which the cells are well separated from each other. In many cases the cells are scarce or occur in groups, and no precise count is possible.

Some testicular cells are present in virtually all specimens of semen with a density of 1,000,000 or more sperms per ml. They are sometimes present in azoospermic semen, in which they may represent the only evidence of patency of the ducts. Generally speaking, testicular cells are numerous only where spermatogenesis is in evidence; and in such cases up to 20,000,000 cells per millilitre may be found, so that the microscopical picture is dominated by them.

For clinical purposes the density of testicular cells may be roughly graded as follows: Grade I, not more than 10,000 cells per ml.; Grade II, 10,000–50,000 cells per ml.; Grade III, 50,000–300,000 cells per ml.; Grade IV, more than 300,000 cells per ml.

The relationship between testicular exfoliation and fecundity has been emphasized by Joël (1942) and others. It is further illustrated in Table I, which relates to some random samples. Generally speaking, pronounced testicular exfoliation is relatively uncommon in semen of proved or probable fecundity, though we have found that even a high degree of exfoliation is compatible with fertilization. Conversely, intensive exfoliation is fairly common in subfecund men. The rarity of testicular cells in azoospermic semen reflects the most common causes of azoospermia—a low degree of proliferation of the seminiferous epithelium or occlusion or functional impairment of the ducts.

TABLE I.—*Frequency of Various Degrees of Exfoliation in Relation to Fecundity*

Character of Semen	No. of Cases	Grade I	Grade II	Grade III	Grade IV
Fecund ..	50	72%	10%	8%	10%
Subfecund* ..	37	51·4%	5·4%	24·5%	18·8%
Azoospermic ..	41	90·2%†	4·8%	4·8%	0

* For criteria of subfecundity, see text.
† In the majority of these cases no testicular cells were identified ("acytospermia") (see text).

Clinical Significance and Biological Background of Exfoliation

It seemed likely that the causes of testicular exfoliation were also responsible for the associated infecundity. In considering possible endocrine causes we took into account the fact that a considerable number of subjects had received endocrine treatment—for example, serum-gonadotropin, testosterone—before the present study was undertaken, without showing significant diminution of exfoliation. It was also noted that exfoliation may be associated with the formation of numerous normal motile spermatozoa and with the production of apparently normal seminal fluid, either of which depends upon adequate secretion of testosterone. Nor is there any other evidence that exfoliation reflects specific endocrine deficiencies. Thus hypophysectomy in animals results in inactivity of the seminiferous epithelium, but not in the epithelial disorganization combined with proliferation reflected by exfoliation.

A more likely explanation suggested itself from experimental and other findings. Numerous authors have described testicular changes in animals resembling those seen in human cases of exfoliation and caused by widely different unspecific factors. Such derangement of spermatogenesis occurs in man and animals after pyrexia or experimental increase of scrotal temperature, under the influence of emotional strain, and in certain nutritional deficiencies. Again, infections, whether genital or not, ingestion of certain organic compounds, exposure to *x* rays, and severe physical trauma may produce the same condition (see references marked with a dagger). Experimental data also suggested that the damage resulting in excessive exfoliation need not be permanent and that recovery of the epithelium with increased fecundity may occur when the noxa has been eliminated.

Clinical observations also suggested a corresponding approach to the problem of exfoliation in human subjects. Several highly fecund subjects submitted specimens of semen at intervals during the last eight years. In these, exfoliation was normally limited to a few cells or was virtually in abeyance. But in three of these subjects pronounced exfoliation occurred during transitory illness, only to disappear spontaneously within two to three months. The role of unspecific noxae in the causation of exfoliation was further borne out by observations in infecund men in whom infective or toxic conditions were present.

In the past six years nearly 200 cases of infecundity combined with exfoliation were investigated and where possible treated. The primary investigation involved the usual semen, post-coital, and invasion tests. The following characteristics, occurring singly or in conjunction, were regarded as signs of lowered fecundity: (*a*) oligozoospermia (fewer than 15,000,000 per ml. seminal fluid); (*b*) asthenozoospermia; (*c*) gravely impaired invasive capacity as shown with ovulatory invadable mucus; and (*d*) pyospermia or severe and rapid agglutination of spermatozoa. High frequency of abnormal head forms was not by itself regarded as a criterion for inclusion in the group. Where routine clinical examination suggested possible sources of toxic absorption or other potential testicular noxae—for example, metabolic disturbances—treatment for these was advised. Where no such likely cause presented itself the patient was referred for more specific investigation, and treatment was advised in the light of the results. Where extended search failed to reveal any definite abnormality, treatment was either abandoned or some purely tentative measures were undertaken. Treatment was generally carried out by the patient's own doctor.

Criteria of Effectiveness of Therapy.—Only marked and persistent reduction of exfoliation which necessitated classification of the semen in a lower grade was regarded as significant. Fecundity was regarded as improved only if the stigmata mentioned above were eliminated. The occurrence of conception alone was not regarded as evidence of adequate response, since even severe infecundity occasionally permits of fertilization. Many subjects display a comprehensible but annoying disinclination towards further investigation once conception has occurred.

The results of treatment varied widely, as illustrated by abstracts from case histories.

Case 1, Showing Response to Treatment

Subject aged 32, married seven years; wife aged 30. No contraceptives used. No conception. Effective duration of marriage reduced to about two years through war service. Patient was prisoner of war for three years.

First specimen of semen: volume 2.5 ml.; density, 3,000,000 spermatozoa per ml.; about 27% severely abnormal head forms, including 7% duplex forms; initial motility, 35% (paraffin film); viability, 2% survival six hours after emission, room temperature. Exfoliation of testicular cells marked (Grade III); mostly small mononuclear, with some binuclear cells. No polymorphs. In the following three months second and third specimens showed similar findings, with invasive capacity gravely impaired. Sims post-coital test: cervical invasion virtually absent.

Clinical findings: tall, asthenic man with history of furunculosis (generalized boils) of three years' duration. No other abnormalities. Bacteriological findings (semen, urine, throat): no pathogens recovered.

Advised to have (as a first step) treatment for furunculosis. Responded well to treatment.

Two months later, before other measures could even be considered, the wife's menstrual period was overdue, the temperature level luteal, and the pregnancy test positive. The semen then showed a volume of 1.8 ml.; approximately 4,000,000 per ml., with high initial motility. Viability: about 20% motile six hours after emission. Exfoliated cells virtually absent. Considerable gain in weight. No skin complaint.

The pregnancy went to term. No relapse occurred in the subject's condition during the next two years. The child is healthy and a second pregnancy has now gone to term.

Case 2, Illustrating Absence of Response

An accountant aged 49, married 13½ years, wife aged 38. No conception. A semen test two years previously by another investigator showed 29% abnormal head forms and poor motility, many testicular cells and pyospermia, and 17,000,000 spermatozoa per ml. He was then given testosterone, also by another physician. A repeat test by the same investigator ten months later showed no definite changes. He was then given a course of penicillin (no cultures taken), again without seminal response. He was then seen by one of us (M. B.) and the semen was found to be subfecund—21,000,000 spermatozoa per ml. Motility after three hours, 21%. There was unusually heavy exfoliation of testicular cells (Grade IV), with predominance of spermatocytes in arrested division, also some prostatic cells and pus cells in large numbers (pyospermia). A semen inoculum on blood agar showed a moderate growth of *Bact. coli*.

Clinical findings: normal build; very pallid complexion. No abnormalities found. No relevant history. He received a course of sulphadiazine, and simultaneously his wife was treated for an infected cervix with impaired invadability. There was no significant change in the semen after the course of sulphadiazine; but conception took place, with spontaneous miscarriage in the seventh week of gestation. Without further treatment a second conception occurred during the first cycle following upon abortion. However, abortion took place again at six weeks. The semen at that time still showed excessive exfoliation (Grade IV). The cells were mostly well-preserved spermatocytes and other mononuclear cells, including spermatids with abortive differentiation. Several million spermatozoa were found, but no precise count could be made because of aggregated testicular cells. A few polymorphs only were present. A semen inoculum (blood agar) remained sterile.

The patient was now given a course of cacodylate, advised on dietary measures, and seen again after a holiday abroad. A semen test two months later showed about 10,000,000 spermatozoa per ml., high viability, approximately 6,000,000 cells per ml. (50% large mononuclears, 12% small mononuclears, 20% large and small binuclear cells, the remainder intermediate forms); 30% of the heads of the differentiated spermatozoa were abnormal. In view of this persistent exfoliation the patient was referred to hospital for full examination (by Dr. P. E. Thompson Hancock). Exhaustive search failed to reveal any abnormality except severe bacilluria (*Bact. coli*). No symptoms. A course of mandelamine was given. Two months later a repeat urine culture remained sterile and the urine was normal. A semen test after a further four weeks showed about 7,000,000 spermatozoa per ml. with high initial motility and high viability, few abnormal forms, but persisting exfoliation of Grade IV with predominance of mononuclear cells. No further tests could be made until four months later, the wife having had further treatment in the meantime. On this occasion the high viability combined with oligozoospermia was noted again, but there were about 20,000,000 cells per ml., including numerous polymorphs (about 38% large mononuclear cells, 11% small mononuclears, 7% large binuclears, 11% small binuclears, 19% multinuclears, and 15% polymorphs). At this time the wife suffered a relapse of cervical infection and had a further course of antibiotics, but in view of the husband's seminal condition and the likelihood of repeated abortion the couple were advised to discontinue specific treatment to procure conception. Eighteen months later no further conception was reported.

Summary of Results

In about three-quarters of our cases definite pathological conditions were detected, though they were not always reflected by subjective complaints and were often of the "subclinical" type. Most commonly they were seemingly localized infective conditions such as bacilluria or chronic sinusitis.

Effective attention to such conditions resulted in reduced exfoliation and improved fecundity in about one-third of the cases.

On the other hand no potential noxa was discovered during the period of investigation in about one-quarter of the cases. In some of the latter purely empirical and tentative measures such as dietary correction were followed by response, possibly reflecting an improvement in general health.

We satisfied ourselves that specific hormone therapy should always be postponed until exfoliation has at least begun to decrease and that premature efforts to increase invasive power and viability of spermatozoa by such means are likely to fail.

The results are illustrated in greater detail in Tables II and III, which relate to 50 successive cases.

TABLE II.—*Clinical Rating of Cases in Relation to Effect of Treatment*

	Total No.	Exfoliation after Treatment		
		Significantly Reduced	Not Significantly Affected	Increased
Systemic abnormalities detected (Group A):				
Group A as a whole ..	38 (76%)	21 (42%)	14 (28%)	3 (6%)
Group A, fecundity improved	15	12 (24%)	3 (6%)	0 (0%)
Group A, fecundity not improved ..	23	9 (18%)	11 (22%)	3 (6%)
Systemic abnormalities not detected (Group B):				
Group B as a whole ..	12 (24%)	3 (6%)	8 (16%)	1 (2%)
Group B, fecundity improved	3	2 (4%)	1 (2%)	0 (0%)
Group B, fecundity not improved	9	1 (2%)	7 (14%)	1 (2%)

TABLE III.—*Summary of Table II*

	Exfoliation Significantly Reduced	Exfoliation Not Reduced
Fecundity improved ..	14	4
,, not improved ..	10	22

Control Data.—Exfoliation, though occasionally of a temporary nature, usually persists in untreated cases. Twelve of the subjects included in the present series had been infecund for fairly long periods before the present study began; during this period semen tests were carried out, and in some instances endocrine treatment was given; yet the condition of the semen remained virtually unchanged, exfoliation persisting. Positive responses were observed in seven of these men.

Conclusions and Comments

1. The present findings support the view that the pathological process of excessive testicular exfoliation commonly reflects a systemic "load." This conclusion is not invalidated by the failure to identify the causative noxa in any one case, for clinical and biological investigation is necessarily limited by available methods and by circumstances. Furthermore, some testicular noxae—for example, vitamin-E deficiency (Mason, 1933)—produce irreversible changes and may no longer be discoverable at the time of investigation. The demonstration of systemic noxae does not exclude purely local factors—for example, local effect of heat.

2. Since there is little doubt that testicular "sloughing" is commonly associated with infecundity special attention should be paid to the presence of testicular cells in the semen. This applies even to specimens where other general features indicate fecundity; for it is our impression that exfoliation in such cases may presage decline in other respects—for example, fall in the spermatozoa count. But semen analysis cannot determine the line of treatment to be pursued, and the therapeutic advice which in recent years has often been expected from the "seminologist" properly belongs to the physician.

3. Most experiments with antimitotic agents have been concerned with the effect of *exogenous* mitotic poisons—for example, stilboestrol, benzoquinone, benzene—upon embryonic tissues, meristem, bone marrow, and other rapidly proliferating cell systems (cf. Toeppner, 1941; Lehmann, 1947). It is therefore of some interest that the seminiferous epithelium may also reflect the antimitotic action of *endogenous* factors. Its reaction resembles that of the bone marrow, which, under the influence of certain antimitotic agents and in disease, produces cells bearing a striking resemblance to binuclear and multinuclear testicular cells—cf. illustrations given by Leitner (1949) and by Schleip and Alder (1928).

4. Lastly the antimitotic nature of some testicular noxae suggests certain tentative conclusions which, though theoretical, deserve to be mentioned. The exposure of the testis of the mouse to *x* rays at certain antimitotic dosage levels has a twofold effect upon fertility. First, ova fertilized by males soon after irradiation—that is, by spermatozoa which were hit by *x* rays—show low viability and the number of young produced is abnormally small. Secondly, this infertility or "reduced prolificacy" (Tyler and Chapman, 1948) is transmitted to the surviving offspring, so that a hereditary and dominant form of infecundity is produced. Irradiated mice may regain full fertility, with normal prolificacy in their offspring, if allowed a period of recovery during which the seminiferous epithelium can regenerate from unaffected spermatogonia (Hertwig, 1938).

It is as yet uncertain whether other antimitotic agents, such as those which are involved in exfoliation in our cases, may produce a similar effect upon prolificacy. But the possibility must be borne in mind and requires further investigation, *particularly since the histological pictures in the testis of the mouse after irradiation and that in the human testis in severe exfoliation from other causes* are in some respects very similar. Furthermore, we have some evidence of the reduced viability of human zygotes produced from semen showing severe exfoliation (high incidence of miscarriage). Until further information is available it might be wise to advise against attempts to procure conception from men with signs of severe and unrelenting antimitotic effects.

Summary

Persistent exfoliation of testicular cells, including abnormal cell forms, is often associated with infecundity, though it is compatible with the occurrence of fertilization. It does not respond to specific endocrine measures, but does respond in a significant proportion of cases to the treatment of associated systemic conditions such as metabolic disturbances or infective states.

Reduction of exfoliation is often accompanied by an increase in fecundity.

Some exfoliated cells reflect disturbances of cell division, and it is concluded that endogenous as well as exogenous factors may act as antimitotic agents and possibly produce genetic changes.

It is suggested that in subjects in whom antimitotic effects are much in evidence attempts at reproduction might wisely be postponed in view of the possible danger of hereditary subfertility.

We wish to express our thanks to Mr. Kenneth Walker, who carried out most of the testicular biopsies referred to in this study; to Dr. R. Gottlieb for references to the haematological literature; and to Dr. H. G. Close, West Hill Hospital, Dartford, for lending the specimen used for Figs. 1, 2, 3, and 4. We are particularly indebted to Dr. R. C. Matson, Pathologist, Royal Surrey County Hospital, for carrying out numerous pathological investigations in many of the cases referred to in this communication.

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ENDOTRACHEAL INSUFFLATION WITH OXYGEN IN THE TREATMENT OF ASPHYXIA NEONATORUM

BY

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The present state of our knowledge of the oxygen and carbon dioxide economy of the newborn gives every support to the belief that the chief therapeutic need in severe asphyxia neonatorum is for oxygen, and that the particular means by which this is administered is of less importance, provided it is efficient. The assessment of any one method of resuscitation is of course hard to establish. In the first place there is the difficulty of finding a sufficiently large number treated according to one routine; in the second place there is the impossibility of obtaining an adequate control series either from another hospital or in the same hospital if the routine is felt to be of value.

For these reasons we are recording briefly the long-term results of treating 66 severely asphyxiated infants by endotracheal insufflation with oxygen. These cases occurred from 1949 to 1951, during which time there were 5,458 deliveries.

Methods

The methods employed have already been reported in full by one of us (Roberts, 1949), and may briefly be restated as follows. Whenever possible a member of the medical staff was present to care for the infant when asphyxia was anticipated. In addition there was a resident paediatric registrar on call, who, with the anaesthetists and obstetricians, was versed in the technique of endotracheal insufflation. In all babies the mucus was aspirated from the pharynx immediately after birth; those who did not breathe immediately were then placed head down in a Roberts–Talley infant oxygen rocker. Where respiration had not started by three minutes after birth, a small metal airway was inserted and the infant rocked. The group reported here consists of those who after a further three minutes' rocking—that is, six minutes altogether from birth—still showed no response. The pharynx was then aspirated under direct vision, using an infant laryngoscope, and a No. 00 Magill endotracheal tube inserted. This was attached to a Y-shaped metal connexion which enabled the operator to apply oxygen at intermittent pressures of about 20 cm. of water by occluding the open end for periods of approximately three seconds between 10 and 15 times a minute. The optimum rate of flow for this purpose was 1½ litres a minute. It was found to facilitate the insertion of the tube through the glottic opening if it was threaded with 10-amp. copper fuse wire for about seven-eighths of its length. This allowed the curve of the tube to be maintained.

Insufflation was maintained for as short a time as possible and the tube was withdrawn as soon as respiration began. This interval varied from 3 to 40 minutes, but was usually about seven minutes.

Results

Altogether 66 infants were intubated; of these 14 died. The causes of death are given in the accompanying Table. The remaining 52 infants made an uninterrupted recovery, although two showed transient signs of cerebral irritation in the first 10 days of life—one mild, and one severe enough to be diagnosed as a cerebral haemorrhage. As it is not possible in the immediate post-natal period to assess either the duration of intrauterine anoxia or the possible permanent damage to the central nervous system, we decided to institute a long-term follow-up of this group. It seemed just possible that by waiting as long as six minutes we might be exposing these infants unduly to the risk of subsequent mental debility.

Table Showing Causes of Death

Case	Maternal Complication	Delivery	Birth Weight lb. oz.	Time of Death	Post-mortem Findings
		A. Cases Other Than Asphyxia			
1	Pre-eclamptic toxaemia	1st twin, caesarean	6 1	9 mths	Pneumonia
2	Infectivehepatitis; fibroids	Caesarean	3 12	3 wks	Extensive hepatic necrosis
3	Pre-eclamptic toxaemia	Spontaneous vertex	4 4	31 days	Gastro-enteritis
		B. Asphyxia a Contributory Cause			
4	Nil	Difficult vertex	9 4	1½ hrs.	Congenital urethral valve; gross ascites; hydroureter, hydronephrosis; atelectasis
5	Carcinoma	Therapeutic hysterotomy at 26 weeks	2 13	5 hrs.	Extensive atelectasis
11	Nil	Vertex; cord round neck	6 8	15½ hrs.	Extensive pneumonia
13	,,	Breech	5 0	3 days	Capillary haemorrhage in right parietal region; minimal atelectasis
14	,,	2nd twin, vertex; prolapsed cord	4 0	4 ,,	No necropsy
		C. Asphyxia the Principal Cause of Death			
6	Premature rupture membranes	Spontaneous vertex	2 5	1 hr.	Extensive atelectasis
7	Severe pre-eclamptic toxaemia	Caesarean	4 0	2 hrs.	Partial atelectasis; some subpleural emphysema
8	Nil	Forceps for foetal distress	7 2	5 ,,	Moderate atelectasis; vascular engorgement in thalamic region
9	Antepartum haemorrhage due to placenta praevia	Caesarean	3 6	8 ,,	Aspiration of amniotic contents; atelectasis
10	W.R. positive	Breech, 2nd twin	4 10	16 ,,	Widespread aspiration of amniotic fluid and pulmonary interstitial haemorrhage
12	Severe pre-eclamptic toxaemia, uterus bicornis	Caesarean	4 7	21 ,,	Pulmonary oedema from extensive aspiration; hyaline membranes

The results of this part of the investigation are as follows. It was found impossible to trace six infants. Three infants were below 3 months of age and were not developmentally tested. None of these had shown signs of cerebral irritation or locomotor disturbance during their stay in hospital. The remaining 43 infants were examined clinically, and their degree of development was tested by one of us (D. O'B.), using the technique of Gesell and Amatruda (1949). All of these children appeared normal in every way, except two who from shyness or unfamiliarity with the surroundings co-operated indifferently at the first examination. These two were subsequently re-examined by an independent observer and adjudged normal.

Discussion

Although in this series we feel that our intervention undoubtedly saved the lives of a number of profoundly asphyxiated infants, we are not in a position to prove it. However, where recovery occurred it has been uncomplicated by any permanent cerebral damage. Similar results have been obtained in another study (Usdin and Weil, 1952),

although only 9 of their 40 reported cases would have been included in our group. Of the 14 deaths three were from causes other than asphyxia, and two more—a therapeutic abortion and another with a gross congenital abnormality—would very probably have occurred whatever methods were employed. Of the remaining nine fatal cases, seven responded initially to insufflation, although they died later after periods ranging from five hours to four days with varying degrees of atelectasis and evidence of amniotic aspiration. Of the two who failed to respond, one was a very small premature infant and the other was the only case to show a mild degree of subpleural emphysema.

We have in addition tried to obtain information on precisely how insufflation may modify the physical state of the lungs. The rapid oxygenation of the asphyxiated, as shown by skin colour, the movement of the chest wall, and the showers of fine crepitations on auscultation at each insufflation, suggested that the alveoli themselves were being expanded. Unfortunately, we were not able to obtain any radiographic records in the labour wards; a number of photographs, however, were obtained very shortly after death. Two of these are shown (Figs. 1 and 2), and they suggest that a pressure of + 20 cm. of saline is sufficient to produce a considerable degree of alveolar expansion whilst it is exerted.

FIG. 1.—Case H. Birth weight 4 lb. (1.8 kg.). Control picture showing extensive atelectasis.

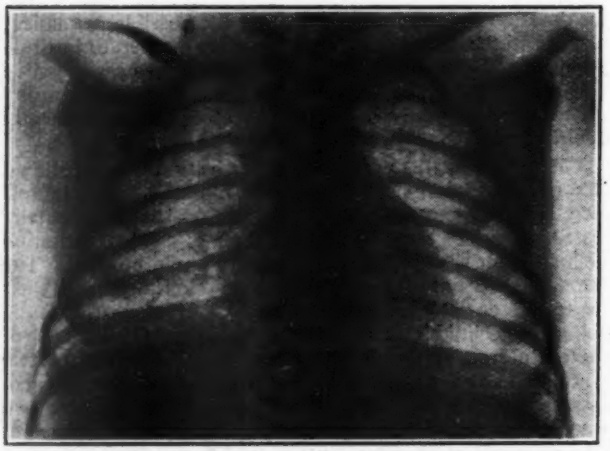

FIG. 2.—Same infant as in Fig. 1, showing alveolar expansion with a sustained intratracheal pressure of +20 cm. of saline.

In addition we have practised this technique in eight very small premature infants who appeared to be dying as a result of atelectasis, in one case continuing for eight hours. In all these there was a transient recovery, as evinced by a rise in pulse rate and improved colour. Life never seemed to be prolonged more than a few hours, and the manipulations of inserting the tube and changing it when blocked with mucus were badly tolerated. Extensive atelectasis without emphysema was revealed in all cases at necropsy. This information, together with that from the post-mortem reports of babies dying of asphyxia, suggests that endotracheal insufflation with the pressures we have used does not to any perceptible degree facilitate the permanent expansion of the atelectatic lung in the newborn, although it may do so in some dead or stillborn infants, especially if full-term. A satisfactory degree of oxygenation of the blood and tissues can, however, be produced almost immediately.

Finally, we would stress the desirability of an established routine in the treatment of asphyxiated infants. For convenience this may be primarily but not exclusively the responsibility of the anaesthetist, the obstetrician, or the paediatrician. To ensure prompt action in the unexpected emergency all should be proficient in the technique employed.

Conclusions

The administration of oxygen under intermittent positive pressure of up to +20 cm. of water by endotracheal tube is, in experienced hands, a safe, quick, simple, and efficient treatment for severe cases of asphyxia neonatorum.

This procedure, though momentarily expanding the alveoli, does not appear permanently to modify the physical state of the unexpanded newborn lung.

We would like to thank Professor J. C. McClure Browne and Professor A. A. Moncrieff for permission to carry out these investigations on infants under their care, and also Dr. C. Upjohn and Dr. M. W. Arthurton, who intubated many of these babies and assisted in keeping the records. Dr. B. W. Powell, Assistant to the Professor of Child Health, kindly reassessed the developmental age of two infants.

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THE RESPIRATORY EFFECTS OF SALICYLATE

BY

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There is an extensive literature on the effect of salicylates on respiration and on the acid–base balance of the blood. Most observers agree that salicylate causes hyperventilation and a reduction in the carbon dioxide content of the blood. There has been great controversy, with many conflicting reports on the interpretation of these findings: whether salicylate causes a primary respiratory alkalosis or a metabolic acidosis with secondary hyperventilation (Johnson, 1930; Morris and Graham, 1931; Rapoport and Guest, 1945; Reid, Watson, and Sproull, 1950).

It was decided to investigate the respiratory effects of orally and intravenously administered salicylate in the human subject. For this purpose a closed-circuit Knipping type spirometer was used. This apparatus measures oxygen consumption, carbon dioxide output, and depth and rate of respiration. Most previous observations on the effect of salicylates on the respiratory movements in the human subject have been made

by clinical assessment, and it was thought that a spirometer record might be of value in defining this effect more accurately and at the same time enable the respiratory gaseous exchanges to be studied.

Method

The Knipping spirometer is a modification of the ordinary Benedict–Roth type, so that it is possible to show on the same record the volume of CO_2 produced as well as the volume of O_2 consumed. By using a rotary airpump to ventilate the apparatus no valves are necessary. Included in the circuit is a special flask which holds potassium hydroxide solution to absorb CO_2. At the top of the flask is a container for sulphuric acid, which is released through a stopcock when it is desired to ascertain the CO_2 produced. It was found at first that CO_2 tended to accumulate in the apparatus, and this resulted in hyperventilation. By trial and error the optimal conditions for satisfactory absorption of circulating CO_2 were established. For a 10-minute spirometer tracing a relatively fast pump-speed of about 870 r.p.m. and 150 ml. of 2.5/N KOH solution are required. The output of air by the pump at this speed is about 33 litres a minute, and to prevent leaks the mouthpiece and noseplug must be carefully and securely fitted.

Experiments were carried out on five healthy young adult male volunteers and on four patients, three with subacute rheumatism and one with rheumatoid arthritis in a quiescent state.

The healthy subjects and the rheumatoid patient came into hospital the night before the experiment, and in the morning were given a standard breakfast of a cup of tea and a slice of toast. In two of the healthy subjects and in the rheumatoid patient two or three control 10-minute spirometer tracings were recorded, and then an intravenous drip of sodium salicylate (10 g. in 400 ml. of distilled water) was given over a period of three to four hours. During the intravenous drip, at approximately half-hour intervals, 10-minute spirometer tracings were taken. The remaining three healthy subjects served as controls. They were given no intravenous drip, but in every other respect were treated like those who received salicylate.

The three subacute rheumatic patients had been sent into hospital as cases of rheumatic fever. On admission they were found to be afebrile and free from carditis, and the only abnormal finding was pain on movement of one or two joints. They were confined to bed and received a standard breakfast. Each morning at a constant time three consecutive five-minute spirometer tracings were taken and the results averaged. When a satisfactory baseline had been obtained oral treatment with aspirin was started in doses of 1½–2 g. five times a day, and morning tracings were continued until treatment was stopped and the respiratory changes returned to the previous control values.

In all subjects occasional blood samples were taken for plasma salicylate determinations.

Results

In the three healthy subjects who acted as controls for the intravenous salicylate experiment it was found that the oxygen consumption and carbon dioxide output remained fairly constant throughout the day (Table I). In each subject there were variations in O_2 consumption and CO_2 output of 20–40 c.cm. a minute, and the respiratory quotients varied by 0.05–0.15. However, no definite sequence of changes was observed, and it was clear that serial tracings at approximately half-hour intervals did not increase O_2 consumption or CO_2 output, and depth and rate of respiration remained constant within narrow limits.

TABLE I.—*Serial Spirometer Results at Half-hourly Intervals Throughout a Four- to Five-hour Period in Three Healthy Young Adults*

30-min. Intervals (approx.)	A. S.					A. R.					I. McD.				
	O_2 c.cm./ min.	CO_2 c.cm./ min.	R.Q.	Tidal Air c.cm.	Resp. Rate /min.	O_2 c.cm./ min.	CO_2 c.cm./ min.	R.Q.	Tidal Air c.cm.	Resp. Rate /min.	O_2 c.cm./ min.	CO_2 c.cm./ min.	R.Q.	Tidal Air c.cm.	Resp. Rate /min.
1	333	247	0·74	600	16	288	252	0·88	850	9	330	265	0·80	810	12
2	300	240	0·80	550	17	275	249	0·90	630	13	297	260	0·88	830	9
3	323	249	0·77	600	16	290	232	0·80	700	10	267	240	0·90	730	9
4	317	246	0·78	580	17	285	237	0·83	690	11	272	260	0·95	800	10
5	317	255	0·80	570	18	285	245	0·86	770	9	280	241	0·86	800	9
6	315	249	0·79	560	17	267	215	0·81	730	8	252	245	0·97	840	10
7	315	247	0·78	550	17	292	218	0·75	650	10	258	254	0·98	800	11
8	318	256	0·81	600	17	275	225	0·82	630	12	253	238	0·94	730	10
9											280	241	0·86	750	10
10											268	251	0·94	800	10

TABLE II.—*Serial Spirometer Results in Two Healthy Adults and in One Rheumatoid Patient (R. A.) who Received Sodium Salicylate by Intravenous Drip*

A. R.*							R. A.†							H. D.‡						
Time	O_2 c.cm./ min.	CO_2 c.cm./ min.	R.Q.	Tidal Air c.cm.	Resp. Rate /min.	Plasma Sal. mg./ 100 ml.	Time	O_2 c.cm./ min.	CO_2 c.cm./ min.	R.Q.	Tidal Air c.cm.	Resp. Rate /min.	Plasma Sal. mg./ 100 ml.	Time	O_2 c.cm./ min.	CO_2 c.cm./ min.	R.Q.	Tidal Air c.cm.	Resp. Rate /min.	Plasma Sal. mg./ 100 ml.
a.m.							a.m.							a.m.						
9.14	313	248	0·79	730	11		9.44	258	222	0·86	630	14		9.27	270	236	0·87	550	14	
9.34	322	231	0·72	700	10		10.4	267	230	0·86	600	14		9.48	283	256	0·90	630	13	
9.52	312	248	0·79	800	9		10.24	248	228	0·92	660	15		Means	277	246	0·89	590	14	
Means	316	242	0·77	740	10		Means	258	227	0·88	630	14		10.57	337	287	0·85	710	16	
10.56	310	247	0·80	780	11		11.29	267	244	0·91	780	16		11.21	362	280	0·77	650	16	
11.33	318	257	0·81	720	11		11.59	292	256	0·88	740	16		11.43	382	278	0·73	710	16	
11.52	335	255	0·76	700	14		p.m.							p.m.						
p.m.							12.35	295	263	0·89	890	16		12.20	418	295	0·71	610	20	18
12.23	377	265	0·70	750	12	22·5	1.15	322	273	0·85	850	18		1.15	480	325	0·68	760	19	27
1.15	429	322	0·75	890	15		1.48	368	272	0·74	880	15		2.0	467	303	0·65	650	20	
2.0	460	316	0·69	900	14		2.17	372	268	0·72	1,080	16		2.28	445	310	0·70	720	19	
2.25	502	363	0·72	1,100	15	38·0	2.35	422			1,050	17	63	3.36	447	300	0·67	680	19	
3.10	467	312	0·67	1,070	12															
3.40	497	321	0·65	1,100	12															
4.48	453	301	0·65	950	12															

* From 10.56 a.m. to 2.25 p.m. Case A. R. received 8 g. of salicylate in 325 ml. of distilled water intravenously.
† From 11.29 a.m. to 2.35 p.m. Case R. A. received 10 g. of salicylate in 400 ml. of distilled water intravenously.
‡ From 10.57 a.m. to 1.15 p.m. Case H. D. received 7.5 g. of salicylate in 300 ml. of distilled water intravenously.

TABLE III.—*Daily Spirometer Results in Three Patients with Subacute Rheumatism who Received Aspirin by Mouth*

J. McL.*							B. E.†							J. McM. ‡						
Day	O_2 c.cm./min.	CO_2 c.cm./min.	R.Q.	Tidal Air c.cm.	Resp. Rate /min.	Plasma Sal. mg./100 ml.	Day	O_2 c.cm./min.	CO_2 c.cm./min.	R.Q.	Tidal Air c.cm.	Resp. Rate /min.	Plasma Sal. mg./100 ml.	Day	O_2 c.cm./min.	CO_2 c.cm./min.	R.Q.	Tidal Air c.cm.	Resp. Rate /min.	Plasma Sal. mg./100 ml.
1	242	192	0·79	400	24		1	228	219	0·95	360	21		1	282	242	0·86	490	21	
2	237	177	0·75	380	22		2	228	205	0·90	390	20		2	251	244	0·96	480	23	
3	237	190	0·80	440	20		5	226	203	0·90				3	266	266	1·0	590	21	
6	227	191	0·84	450	21		6	224	199	0·89	390	22		4	270	277	1·0	610	22	
7	223	185	0·83	470	20		Means	227	207	0·91	380	21		5	257	234	0·94	500	23	
Means	233	187	0·80	430	21		7	236	223	0·94	470	21		6	275	259	0·93	540	20	
8	237	200	0·84	590	19		8	245	221	0·90	500	19		8	294	283	0·97	560	19	
9	279	211	0·76	650	20		9	262	208	0·80	490	18	25	9	289	281	0·97	630	19	
10	276	218	0·79	830	19		12	233	197	0·86	420	18		Means	273	260	0·95	550	21	
13	317	209	0·66	940	21	40	13	222	192	0·87	420	16		10	297	280	0·94	750	16	
14	260	214	0·82	770	19		14	246	214	0·88	440	18		11	345	307	0·89	930	17	42
15	209	187	0·89	540	18		15	230	202	0·88	440	18		12	386	309	0·80	1,000	16	49
16	199	180	0·91	510	17		16	221	190	0·86	390	18		13	300	267	0·89	760	13	
17	208	173	0·84	500	15		19	220	202	0·90	410	18		15	265	251	0·94	650	13	
20	195	172	0·88	460	17									16	269	245	0·91	620	15	
21	209	188	0·90	480	15															

* From the eighth to the thirteenth day Case J. McL. received 37.5 g. of aspirin orally.
† During the seventh and eighth days Case B. E. received 21 g. of aspirin orally.
‡ During the tenth and eleventh days Case J. McM. received 26 g. of aspirin orally.

Table II shows the results obtained in the two healthy young adult male subjects (A. R. and H. D.) and in the rheumatoid arthritis patient (R. A.), who received sodium salicylate by intravenous drip. The initial control readings are averaged, and these values can be compared with those obtained during and after the intravenous drip. There is a progressive and marked increase in O_2 consumption. When the average value for the control period is compared with the maximum value obtained during the intravenous drip it will be seen that the increase in O_2 consumption per minute for subject A. R. is 186 c.cm. (59% increase), for R. A. 164 c.cm. (64% increase), and for H. D. 203 c.cm. (73% increase). In all subjects the increased O_2 consumption was accompanied by an increased CO_2 elimination, but a disproportion between the levels of O_2 and CO_2 developed, so that the respiratory quotients showed a progressive fall. In two subjects (A. R. and R. A.) the fall in R.Q. did not occur until the intravenous salicylate drip had been in progress for two to three hours, whereas in one subject (H. D.) the R.Q. showed a significant fall within one hour of starting the drip. Hyperventilation was observed in all three subjects. In two (A. R. and R. A.) the tidal air at the time of maximal O_2 consumption had increased from the average control value by 360 and 420 c.cm. respectively, while in subject H. D. hyperventilation was less marked throughout the experiment, and the maximal tidal air was only 170 c.cm. greater than the average control value. In each subject salicylate caused an increase in the rate of respiration, by about four to six respirations a minute. The greatest augmentation of respiratory rate occurred in the subject (H. D.), who showed the smallest increase in tidal air. The results in one subject (A. R.) are shown in graphic form in Fig. 1.

A similar pattern of changes was observed in the three patients who received aspirin by mouth (Table III). The overall increase in O_2 consumption was not so great as in the intravenous experiments. The maximal O_2 consumption exceeded the average control value in patient J. McL. by 84 c.cm. (36% increase), in B. E. by 35 c.cm. (15% increase), and in J. McM. by 113 c.cm. a minute (41% increase). As before, the increase in CO_2 output was not proportional, and this resulted in a fall in R.Q. which was not manifest until the second or third day of treatment. Hyperventilation occurred in all patients within 24 hours of starting treatment, and in two of the patients (J. McL. and J. McM.) the maximal tidal air was approximately double the average control value. The respiratory rate was either unaltered or showed a slight reduction. Fig. 2 illustrates the changes in one patient.

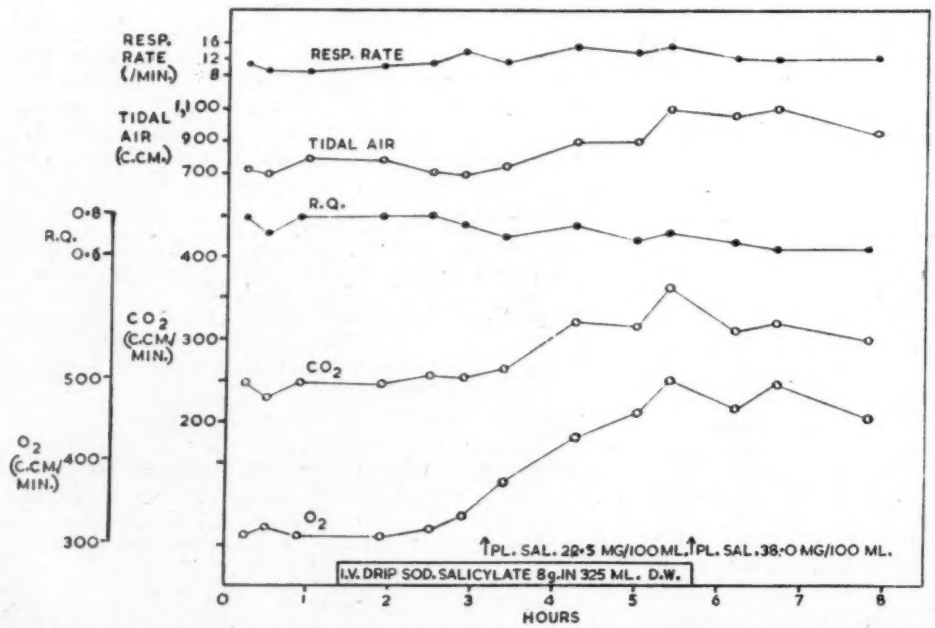

FIG. 1.—A graphic record of the results obtained in one subject (A. R.) who received sodium salicylate by intravenous drip. There is a progressive rise in O_2 consumption and tidal air during the intravenous drip. The respiratory quotient falls owing to a disproportionate rise in CO_2 output.

It will be seen in Figs. 1 and 2 that there is a definite parallelism between the curves of O_2 consumption and tidal air. To eliminate the possibility that deep breathing on the spirometer might potentiate an O_2 leak and thereby cause an apparent increase in O_2 consumption, the effect of voluntary hyperpnoea was compared with normal respiration in two of the subjects who had been used for the oral aspirin experiments. The expected increased elimination of CO_2 was observed, but no increase in O_2 consumption occurred even when the tidal air was almost doubled (Fig. 3).

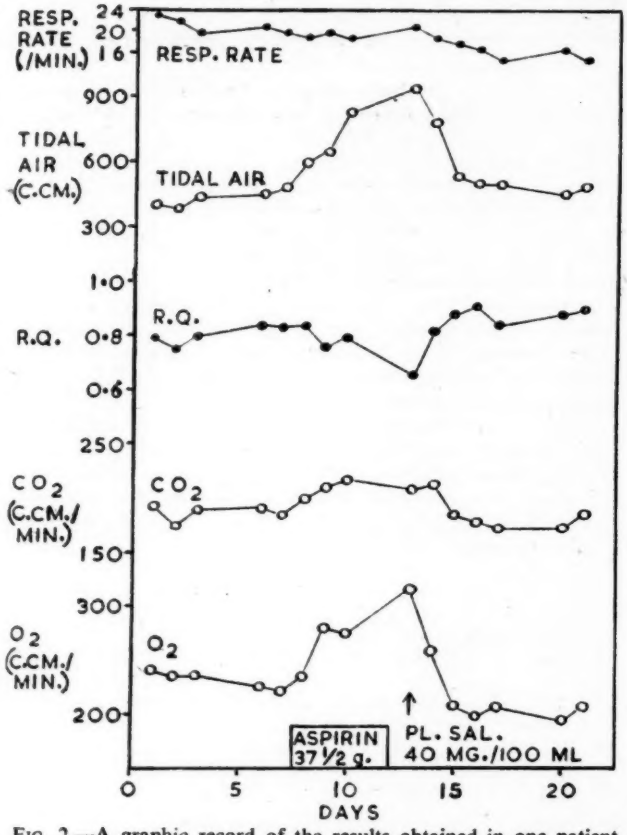

FIG. 2.—A graphic record of the results obtained in one patient (J. McL.) who received oral aspirin treatment. Increased O_2 consumption and tidal air due to aspirin are clearly seen. The rise in CO_2 output is disproportionate and the R.Q. falls.

Discussion

Barbour and Devenis (1919), using a Benedict respiration chamber, showed that aspirin in single doses of 1 g. orally caused a slight increase in metabolism (6.1%) in normal individuals. They also observed a slight increase in CO_2 output, but no alteration in respiratory quotient. In the present investigation there is a marked and progressive increase in O_2 consumption when salicylate is given in full therapeutic dosage to normal and subacute rheumatic subjects.

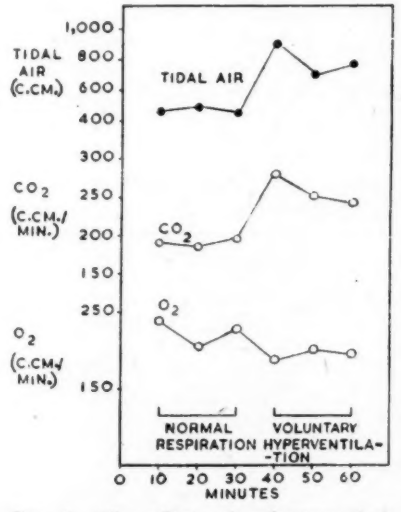

FIG. 3.—The effect of voluntary deep breathing on O_2 consumption and CO_2 elimination in one of the patients (J. McL.) who was used in an oral aspirin experiment. Although the tidal air has been almost doubled there is no increased consumption of O_2. The expected increased elimination of CO_2 occurred.

In the investigations described the maximal increase in O_2 consumption was 30–40% for oral aspirin and 60–70% for intravenous salicylate. In the oral experiments the aspirin dosage and the plasma salicylate levels at the times of maximal O_2 consumption are within ordinary therapeutic limits. In the intravenous experiments the dosage of sodium salicylate used (10 g. in 400 ml. of distilled water in three to four hours) is a little higher than that recommended by Coburn (1943) in the treatment of the active phase of rheumatic fever (10 g. of sodium salicylate in 1,000 ml. of 0.9% NaCl in four to six hours), but again the plasma salicylate levels at the times of maximal O_2 consumption are within ordinary therapeutic limits in two subjects. In the third subject (R. A.) a plasma salicylate level of 63 mg. per 100 ml. occurred at the height of O_2 consumption, and was associated with excessive restlessness, confusion, and nausea. This was the only occasion in the whole of the investigations when toxic effects caused some anxiety. It is noteworthy that increased O_2 consumption occurred early in both oral and intravenous experiments—in the former within 24 hours, in the latter within half to one hour of starting treatment. Insufficient plasma salicylate estimations were done to determine at what level O_2 consumption increased, but in three subjects a definite increase had occurred at levels of 20–30 mg. per 100 ml.

The increased O_2 consumption following salicylate must be due to an increased metabolic rate. As regards the particular metabolite or metabolites affected, the observed fall in R.Q. would suggest that protein and/or fat is being predominantly combusted. In each subject studied the R.Q. showed a progressive fall during the period of salicylate therapy and reached its lowest level about the time of maximal oxygen consumption. There are numerous reports in the literature concerning the effect of salicylate on carbohydrate and protein metabolism. Hyperglycaemia and glycosuria have often been described in cases of salicylate poisoning, and Morris and Graham (1931), from a study of the effect of salicylate in the fasting blood-sugar level in rheumatic children, conclude that the drug inhibits the utilization of glucose by the tissues. Much of the work on protein metabolism has concerned the stimulation of uric acid excretion, but Reid, Watson, and Sproull (1950), from a study of the nitrogen balance in rheumatic patients treated with salicylate, conclude that an important therapeutic action of the drug is to stimulate protein catabolism. The effect on fat metabolism has so far been neglected.

From the present investigation no definite conclusions can be drawn concerning the nature of the metabolic stimulation, and further study is required in both the normal and the rheumatic subject. It is nevertheless believed that the marked and progressive increase in tissue oxidation following salicylate treatment may well be of fundamental importance in the therapeutic action of the drug.

Summary

The effect of orally and intravenously administered salicylate on respiration in the human subject has been studied by means of a Knipping type closed circuit spirometer. In addition to an increase in depth of respiration, the drug caused a marked and progressive increase in O_2 consumption. It is suggested that this latter effect may be of fundamental importance in the therapeutic action of the drug.

I thank Professor Sir John McNee for his advice and generous help in providing facilities for this work. I am greatly indebted to Dr. James Reid and Dr. David Sproull for their criticism and technical assistance throughout the investigations.

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Witch-doctors in South Africa are no longer to be allowed to advertise their magic remedies, according to a report in *The Times* (October 25). The advertisement of medicines containing human ingredients, insects and reptiles, "supernatural legendary and mythical beings," and substances giving protection against "hostile agencies, supernatural powers, witchcraft, or unnatural diseases," will make the practitioner concerned liable to a fine of £50 and six months in prison.

HIGH BLOOD PRESSURE IN THE ELDERLY

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The observations which follow were derived from the medical examinations of 476 elderly people living at home in Sheffield and from the radiological examination of 332 of them. The age- and-sex distribution is shown in Table I. This paper deals only with observations on the blood pressure, the main report will be published elsewhere.

TABLE I.—*Age and Sex*

Years:	60–	65–	70–	75–	All Ages
No. of females	44	105	75	60	284
% of females in each age group	16	37	26	21	
No. of males		39	80	73	192
% of males in each age group		20	42	38	

Series of cases of hypertension as studied in hospital or the doctor's surgery inevitably consist largely of patients with symptoms which have been rightly or wrongly attributed to the raised blood pressure. The present survey included a good many subjects with hypertension without symptoms who considered themselves fit, and, conversely, some without hypertension but with symptoms often ascribed to it. It therefore provided an opportunity of comparing the incidence of certain symptoms and signs commonly associated with hypertension in those with and without hypertension.

The conditions studied in relation to hypertension were vertigo, tinnitus, angina of effort, clinical arteriosclerosis, radiological enlargement of the heart, and the subject's well-being and activity. Data about these conditions were systematically collected in each case. No cases of malignant hypertension or chronic nephritis were found, possibly owing to the age of the subjects, and all the cases of hypertension were regarded as belonging to the benign group. It should be emphasized that only elderly subjects were studied, and the conclusions reached may not apply to hypertension in younger persons.

The Sample

In 1948 a social survey had been carried out by the Sheffield Council of Social Service on a 1:30 sample of all Sheffield old people of pensionable age—that is, women over 60 and men over 65 (Greenlees and Adams, 1950). The sample had been selected by a random procedure from the food office register. The group of elderly people used in the medical survey was derived from this sample and included all those living alone or alone with spouse who could be traced, and who agreed to be examined. Those living alone or alone with spouse were chosen to facilitate a dietary survey which was carried out at the same time. Of 672 possible subjects, 196 were not available when the medical survey came to be done; 36 were no longer living alone or alone with spouse; 18 had left Sheffield or could not be traced; and in 142 cases consent for the examination was withheld. As two years had elapsed between the two surveys, the youngest women in the medical survey were 62 and the youngest men 67.

In the tables the conventional quinquennial age groups have been retained, although this means that the youngest age group in both sexes is smaller than it should be. The sample included all social classes, and we believe was reasonably representative of elderly people living independently at home. Information about frequency of medical attention, obtained at the earlier social survey, showed that those who refused the clinical examination did not differ significantly from those who agreed to it in this respect. This suggests that those who refused did so mainly on other grounds than health. There was a higher proportion of women and of representatives of the higher income groups amongst the refusals. One physician (H. D.) carried out 94% of the medical examinations.

Method.—The blood pressures were taken with a standard mercury sphygmomanometer with the subject in the reclining position after having rested for five minutes or longer. For the study of individual cases a single estimate is unsatisfactory, but in comparing the mean blood pressures of groups the single measurement is less open to objection.

Age and Sex

The distribution of the blood pressures by broad groups is shown in Table II. It will be noted that hypertension was commoner in the women than in the men. Most other authors have found this—for example, Master *et al.* (1943) and Boas (1950).

TABLE II.—*Percentage Distribution of Blood-pressure Readings*

	Systolic, mm. Hg		
	100–159	160–189	190–
187 men	42·8	38·5	18·7
271 women	22·9	48·3	28·8
	Diastolic, mm. Hg		
	0–99	100–	
187 men	71·7	28·3	
271 women	52·4	47·6	

Fifty-seven per cent. of the men and 77% of the women had systolic pressures of 160 mm. Hg or over, and 28% of the men and 48% of the women had diastolic pressures of 100 mm. Hg or more. Howell (1950) found that three-quarters of the Chelsea Pensioners whom he studied had systolic blood pressures of 160 mm. Hg or more.

TABLE III.—*Mean Blood Pressure at Different Ages*

Years:	60–	65–	70–	75–
No. of men		39	77	71
Mean systolic B.P. ..		157·3	166·8	172·8
No. of women	41	100	72	58
Mean systolic B.P. ..	172·8	178·2	178·0	186·0
No. of men		39	77	71
Mean diastolic B.P. ..		89·9	92·5	91·8
No. of women	41	100	72	58
Mean diastolic B.P. ..	98·2	99·5	98·5	100·0

Table III shows the mean systolic and diastolic blood pressures by sex and age. There was a trend towards slightly higher mean systolic blood pressures with advancing age, but analysis of variance showed that the difference in levels between the age groups was not significant.

To obtain a measure of the general trend of systolic blood pressures with age in the ungrouped data, the correlation coefficients were calculated from the individual pairs of values. Neither of these coefficients ($r=0.095$, 0.122, for men and women respectively) was significant.

There was a wide range in the blood pressures. Possibly if there had been a larger number of observations the trend

between the age groups might have been shown to be significant. With regard to diastolic blood pressure there was no trend with age.

While there seems to be agreement that the diastolic blood pressure does not normally rise with age, most authors—for example, Blackford *et al.* (1930), Howell (1942), Russek (1943), and Master *et al.* (1943)—have found higher mean systolic pressures or a higher incidence of high systolic pressures with advancing age after the age of 40.

Hypertension and Vertigo

Vertigo is a common and disabling symptom in the elderly which is often attributed to hypertension. It is commoner in women than in men (Sheldon, 1948). On inquiry we found that 29% of the women and 14% of the men complained of frequent or continuous vertigo. The mean systolic and diastolic blood pressures in those with no vertigo, occasional, and frequent or continuous vertigo are shown in Table IV. It shows that there was no relation between the presence of vertigo and the height of the systolic or diastolic blood pressure.

TABLE IV.—*Vertigo and Blood Pressure*

	Vertigo		
	None	Occasional	Frequent or Continuous
No. of men	87	74	25
Mean systolic B.P.	166·6	169·3	165·8
No. of women	103	87	81
Mean systolic B.P.	178·0	177·4	182·0
No. of men	87	74	25
Mean diastolic B.P.	91·0	92·2	92·6
No. of women	103	87	81
Mean diastolic B.P.	99·0	99·1	99·3

Hypertension and Tinnitus

Tinnitus in the elderly, like vertigo, is not infrequently attributed to a high blood pressure. Nine per cent. of the men and 10% of the women complained of having tinnitus continuously. Analysis of variance showed that there was no significant difference between the blood-pressure levels in those with continuous, occasional, or no tinnitus (Table V).

TABLE V.—*Tinnitus and Blood Pressure*

	Tinnitus		
	None	Occasional	Continuous
No. of men	115	56	16
Mean systolic B.P.	167·2	163·2	180·0
No. of women	163	77	28
Mean systolic B.P.	179·2	180·6	168·6
No. of men	115	56	16
Mean diastolic B.P.	91·6	91·4	93·0
No. of women	163	77	28
Mean diastolic B.P.	99·5	98·8	97·1

Hypertension and Angina of Effort

Hypertension and angina of effort are often found together in elderly people, and some authors—for example, Bell and Clawson (1928)—are of the opinion that coronary sclerosis is more frequent in hypertensive than in non-hypertensive persons. Of our subjects, 69% had systolic blood pressures of 160 mm. or above, and 30% of these complained of various degrees of angina of effort, compared with 28% in the whole sample. Table VI shows that the mean systolic and diastolic blood pressures in both men and women were somewhat higher in those with angina, but the differences were not statistically significant.

TABLE VI.—*Angina of Effort and Blood Pressure*

	Angina		Statistical Significance	
	Absent	Present	S.E. of Difference	t
No. of men	129	51		
Mean systolic B.P.	164·0	171·0	5·09	Not sig. on 5% level
No. of women	186	74		
Mean systolic B.P.	177·0	183·0	4·54	Not sig. on 5% level
No. of men	129	51		
Mean diastolic B.P.	91·0	94·0	2·9	Not sig. on 5% level
No. of women	186	74		
Mean diastolic B.P.	98·0	100·0	2·2	Not sig. on 5% level

Hypertension and Clinical Arteriosclerosis

It is difficult, if not impossible, to decide on the basis of clinical examination of the arteries whether the intimal or the medial coats are predominantly affected by degenerative processes. Our observations were based on palpation of the radial, brachial, and dorsalis pedis arteries and on ophthalmoscopic examination of the retinal arteries. On the basis of these observations the subject was classified as having marked, moderate, or no arteriosclerosis. The number and percentage of subjects falling in these groups by sex and age are shown in Table VII. It will be seen that the incidence of marked arteriosclerosis in each age group was much higher in the men than in the women. The incidence increased significantly with age in both sexes.

TABLE VII.—*Grades of Clinical Arteriosclerosis by Age and Sex*

	Arteriosclerosis					
	None		Moderate		Marked	
	No.	%	No.	%	No.	%
Men, aged 65–69	2	5·1	16	41·0	21	53·9
,, ,, 70–74	1	1·4	24	32·4	49	66·2
,, ,, 75+	0		13	18·4	58	81·6
Women, aged 60–64	11	28·2	27	69·2	1	2·6
,, ,, 65–69	13	13·4	69	71·1	15	15·5
,, ,, 70–74	4	5·8	37	52·8	29	41·4
,, ,, 75+	1	1·6	17	28·8	41	69·5

χ^2 for increase of marked arteriosclerosis with age was highly significant in both sexes.

The mean systolic and diastolic blood pressures were calculated in the three different grades of arteriosclerosis (Table VIII). There was no significant difference between the mean systolic and diastolic blood pressures in the different grades of arteriosclerosis. Of the women with systolic blood pressures of 160 mm. Hg or above, 33% had marked arteriosclerosis, compared with 29% in those with pressures below 160 mm. Hg. For men the respective percentages were 71 and 68. While the clinical assessment of arteriosclerosis is not very satisfactory, it may be noted that these findings are in conformity with those of various authors who, like Schaaf (1950), regard arteriosclerosis and essential hypertension as primary and independent processes. The fact that marked arteriosclerosis was commoner in the men and hypertension commoner in the women also suggests that the two conditions are not closely associated. Gavey (1949) found no relationship between the height of the blood pressure and arteriosclerosis in the various clinically accessible arteries in his series of old people. Firstbrook (1951), on the other hand, quoting Wilens (1947), states that "severe atherosclerosis is about twice as common in hypertension as in non-hypertension of the same age, sex, and adiposity." Russek (1943) also thought that arteriosclerosis was related to systolic hypertension.

TABLE VIII.—*Arteriosclerosis and Blood Pressure*

	Arteriosclerosis		
	None	Moderate	Marked
No. of men	3	53	128
Mean systolic B.P.	(151·6)	168·3	167·4
No. of women	29	150	85
Mean systolic B.P.	169·2	178·8	182·0
No. of men	3	53	128
Mean diastolic B.P.	(95·0)	94·6	90·6
No. of women	29	150	85
Mean diastolic B.P.	96·4	99·4	99·5

Hypertension and Size of Heart

Chest radiography was carried out in 332 subjects (143 males and 189 females). There was no significant association between the systolic or diastolic blood pressure and the size of the heart estimated from a chest radiograph taken at a distance of 6 feet (1.8 metres). Two independent criteria were used : First, the opinion of the radiologist (J. L. A. G.) on inspecion of the film, and, secondly, the cardio-thoracic ratio (the maximum width of the heart shadow divided by the external width of the bony thorax at that level).

Application of the χ^2 test to the results, shown in Table IX, indicated that enlargement of the heart was not diagnosed by the radiologist significantly more often in those with high blood pressures than in those with low ones. Also the correlation coefficients between the cardio-thoracic ratios and both systolic and diastolic blood pressures were not significant at the 5% level.

TABLE IX.—*Size of Heart (Assessed by Radiologist) and Blood Pressure*

	Systolic		Diastolic	
	0–159	160+	0–99	100+
No. of men radiographed	62	81	107	36
No. with enlarged hearts	11 (17·7%)	20 (24·7%)	21 (19·6%)	10 (27·7%)
No. of women radiographed	46	143	98	91
No. with enlarged hearts	11 (23·9%)	35 (24·5%)	24 (24·5%)	22 (24·2%)

While the numbers are too small to justify a firm conclusion they suggest that hypertension by itself is not an important cause of cardiac enlargement in the elderly.

Hypertension and Fitness

At the end of the examination the subject was asked whether he considered himself fit, moderately fit, or unfit (Table X). The proportion of those in the high-blood-pressure and low-blood-pressure groups who considered themselves fit did not differ significantly.

TABLE X.—*Subjects' Self-assessment of Fitness by Blood Pressure*

	Systolic		Diastolic*	
	0–179	180+	0–99	100+
No. of males in group..	120	67	132	53
No. "fit"	75 (62·5%)	38 (57%)	80 (60·6%)	33 (62%)
No. of females in group	131	138	140	129
No. "fit"	67 (57%)	60 (43·5%)	70 (50%)	57 (44%)

* In two cases diastolic pressure not recorded.

The χ^2 test showed that the differences were not significant at the 5% level of probability.

It seems, therefore, that in this age group there is little association between feeling of fitness and the height of the blood pressure. A further assessment of the relation between hypertension and general health was made by examining the relationship between the blood pressure and the activity of the subject grouped under four headings : (*a*) unlimited outdoor activity ; (*b*) limited outdoor activity ; (*c*) confined to the house ; and (*d*) bedfast. There was no correlation between degree of activity assessed in this way and systolic or diastolic blood pressure.

Correlation Coefficients Between Activity and Blood Pressure

Females (269)	Systolic B.P. ..	r=0·093	Males (186)	Systolic B.P. ..	r=0·052
	Diastolic ,, ..	r=0·109		Diastolic ,, ..	r=0·07

Summary

Clinical examination was made of 192 men and 284 women over pensionable age and living at home in Sheffield. Chest radiography was carried out in 332 who came to hospital for the purpose.

The relationship between resting systolic and diastolic blood pressure and the presence of certain symptoms and signs was examined.

There was no significant correlation between the height of the systolic or diastolic blood pressure and vertigo, tinnitus, angina of effort, clinically detectable arteriosclerosis, radiological size of the heart, or the subject's well-being and activity.

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A SIMPLIFIED BENZIDINE TEST
WITH AN EVALUATION OF SOME FAECAL OCCULT BLOOD TESTS

BY

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An ideal test for faecal occult blood should satisfy two criteria ; (*a*) absolute specificity for blood or its derivatives, and, furthermore, for blood released in the alimentary canal only, as distinct from ingested blood ; and (*b*) ease of performance. Unfortunately, no such test has been devised. The four main methods employed are:

I. Microscopical demonstration of red blood cells (Bloem, 1933).

II. Microscopical demonstration of crystals of a haemoglobin derivative—for example, Teichmann's (1853) haemin test, pyridine-haemochromogen (Kerr and Mason, 1926).

III. Spectroscopic tests demonstrating the presence of haemoglobin or its derivatives (Ryffel and Payne, 1923 ; Snapper and van Creveld, 1927a, 1927b ; Bloem, 1933).

IV. Tests depending upon the power of haemoglobin and its derivatives to oxidize certain chromogenic substances: guaiacum, first performed by Schoenbein (1856) and verified by Day (1867), Kastle (1909), also Weber (1893), and Boas (1901, 1914) ; guaiaconic acid (Schaer, 1898) ; aloin (Schaer, 1900) ; benzidine (Schlesinger and Holst, 1906 ; Schumm, 1907) ; malachite green (Buckmaster, 1908) ; phenolphthalin (Meyer, 1903 ; Kastle and Amoss, 1906 ; Kastle, 1909) : orthotolidin (Ruttan and Hardisty, 1912a, 1912b ; Kirschen *et al.*, 1942) ; and other substances.

Compared with the ideal test, methods I and II satisfy neither criterion. Microscopical demonstration of red blood cells suffers from an additional disadvantage in that bleeding from high up in the alimentary canal cannot be demonstrated, since digestion of the red cells occurs. Further, as Bloem (1933) showed by comparative tests on blood–faeces mixtures, it is only about one-hundredth as sensitive as the benzidine test. Methods II and III are laborious and not practicable outside a laboratory. Bloem found spectroscopy to be

about one-ninth as sensitive as the benzidine test: although the spectrum of haematoporphyrin is not found in faeces following ingestion of meat, it is inhibited by magnesium, calcium, or bismuth preparations, it may be present in pernicious anaemia in the absence of bleeding, and it may be confused with faecal porphyrins in hydroa aestivale (Ryffel and Payne, 1923). Thus for ease of performance we are left with method IV, although none of these tests satisfies the first criterion. Gregersen (1916), however, believing that blood in faeces in a concentration less than 1/3,000 to 1/20,000 was not pathological, modified the benzidine test by reducing its sensitivity (see Koopman, 1921). Ogilvie (1927) demonstrated that Gregersen's test does in fact satisfy the first criterion except after the ingestion of raw bone marrow: it was negative even after a meal containing 3 oz. (85 g.) of raw meat. Unfortunately, Gregersen's reagent consists of a powder containing 0.2 g. of barium peroxide and 0.025 g. of benzidine dissolved in 5 ml. of 50% glacial acetic acid; and the solution requires to be freshly made up each day at least—anything but simple for the clinician, especially outside hospital practice.

The present study of faecal occult blood tests was undertaken to investigate the relative sensitivity of the more popular tests, and their fallacies; the effects of diet and laxatives on the results; the incidence and persistence of positive benzidine reactions following the release of various quantities of blood into the stomach; together with the changes in blood-urea levels and in the colour of the stools. A simplified modification of the benzidine test is introduced and is compared with the usual tests by the above methods; its sensitivity is estimated following the introduction of known quantities of blood into the stomach and small intestine; while, finally, its clinical value and reliability compared with the ordinary benzidine test is assayed in cases of known alimentary bleeding.

Methods

All faecal specimens were obtained from the centre of the stool.

Guaiacum Test.—Solutions of guaiacum resin in industrial spirit in 1, 5, 10, 15, and 20% strengths were compared: 1% was found to be the most sensitive strength, as its paler colour and less dense precipitate enable the appearance of a blue ring to be more easily discerned. Furthermore, it is much less sensitive to enzymes and iron-containing substances. The *B.P.* tincture of guaiac is useless, as, amongst other things, it contains ammonia, which inhibits the reaction.

A piece of faeces the size of a pea was emulsified and boiled for two minutes in 1 ml. of distilled water. After thorough cooling, two or three drops of a 1% solution of guaiac in industrial spirit were added and ozonic ether was run down the side of the tube. The appearance of a blue or blue-green ring at the junction of the fluids was taken as positive. In the presence of minimal quantities of blood a delay of up to 15 minutes may occur.

Benzidine Test.—A saturated solution of benzidine in glacial acetic acid was prepared immediately before each batch of tests. Saturation was assured by the presence of excess undissolved powder. Such a solution will retain its potency for at least eight hours.

A piece of faeces was emulsified, boiled, and thoroughly cooled as above. Three drops of the emulsion were placed into one test-tube and 10 drops into another. Then 1 ml. of saturated benzidine solution was added to each tube. Thereafter, hydrogen peroxide in 10 volumes strength was added slowly, accompanied by vigorous shaking, up to a maximum of 2 ml. The shaking resulted in many tests becoming positive which would otherwise have remained negative. A colour change to green or blue was regarded as positive; a change to a deep purple colour without first becoming green or blue was considered to be negative, although this is often the final colour following a positive result.

Phenolphthalin Test.—The solution used was a commercial preparation of Kastle–Meyer's reagent,* prepared by dissolving 20 g. of potassium hydroxide in 100 ml. of water and adding 2 g. of phenolphthalein; the resulting deep-red solution is boiled with 5–7 g. of zinc dust until the red colour is discharged, and it is then filtered; the filtrate is the reagent. It continues to undergo partial oxidation (the colour darkens) even in a stoppered bottle; this facilitates further oxidation to the colour change and therefore increases the sensitivity of the reagent. It may be decolorized by boiling with zinc dust, which was found to decrease the sensitivity.

A piece of faeces was emulsified, boiled, and cooled as above. The emulsion was made up to two-thirds of a test-tube with distilled water. Then 1 ml. of Kastle–Meyer's reagent was added, followed by one or two drops of hydrogen peroxide (10 volumes strength). The test was regarded as positive if a pink cloud appeared travelling slowly down the tube within one minute. This test is so sensitive that glassware must be chemically clean.

Gregersen's Test.—Prepared powders containing 0.2 g. of barium peroxide and 0.025 g. of benzidine were dissolved in 5 ml. of 50% glacial acetic acid immediately before each batch of tests. The solution remains satisfactory for at least eight hours.

A piece of faeces was smeared on a glass slide, which was laid upon white paper. Some solution was run on to the faeces and the appearance of a green or blue colour within 30 seconds was regarded as positive.

Simplified Modification of the Benzidine Test.—A saturated solution of benzidine in glacial acetic acid was prepared as for the benzidine test. It remains satisfactory for at least eight hours and may therefore be made up in a rubber-stoppered test-tube in the morning and used during the day.

A piece of faeces the size of a pea was put into a short test-tube with an orange stick. Then 1 ml. of saturated benzidine solution was added and the orange stick used to "pound" the faeces in the solution for about half a minute. Another test-tube was two-thirds filled with hydrogen peroxide in 10 volumes strength, and one or two drops of faecal solution were added. Normally, a white cloud appears, sinking to the bottom of the tube. If during its course downwards this cloud (or part of it) becomes green or blue the test is positive. Even the slightest colour change in the cloud is significant. The "trails" of pieces of faeces are considered as part of the cloud. If the drops of faecal solution strike the side of the test-tube before reaching the hydrogen peroxide a green colour will appear at the top. Pieces of faeces themselves may become green or blue in passage downwards through the hydrogen peroxide, and often after reaching the bottom of the test-tube. These phenomena do not indicate a positive result. Faecal matter may be avoided by lining the mouth of the short test-tube with a piece of filter paper and pouring through it—although this becomes unnecessary after a little experience with the test. It is important to observe the cloud against a white background with one's back to the light. If a green or blue colour does not appear in the cloud on its way downwards it will not appear later—in fact a minimal colour change tends to disappear. A time limit is therefore unnecessary.

I. Comparative Sensitivity of the Tests to Dilutions of Fresh Blood in Distilled Water

When additional fluid was added—for example, the distilled water in the phenolphthalin test—the final dilution before addition of the oxidizing agent is quoted. Ten specimens of blood were diluted; all contained more than 14 g.

*As supplied by British Drug Houses Ltd.

of haemoglobin per 100 ml. The maximum dilution detectable in any of the 10 specimens was :

Guaiac	1/30,000
Benzidine	1/48,000
Phenolphthalin	1/8,000,000
Gregersen's	1/16,000
Modified benzidine ..	1/16,000

II. Fallacies in Testing Faeces

(1) The substances shown in Table I were tested, as their presence in faeces is possible.

Note C.—The three patients with unexpectedly positive faecal occult blood tests to Gregersen's and the modified benzidine test are of interest.

(1) A.B. was in hospital suffering from post-encephalitic Parkinsonism. No history of dyspepsia or other gastro-intestinal symptoms was present. Six weeks after the positive test a haematemesis occurred. He was having "artane," 35 mg. daily. The bleeding, clotting, and prothrombin times were normal. Barium examination was not performed, as the patient could not co-operate. Before the haematemesis the blood picture was Hb, 94%; red blood cells, 4,900,000.

TABLE I

	Guaiac	Benzidine	Phenolphthalin	Gregersen	Modified Benzidine
(*a*) Iron medicines: Liq. ferri perchlor. .. .. / Tinct. ,, ,, ... / 1/1,000 ferrous sulphate .. / Mist. ferri et ammon. cit. ..	Positive except F. et ammon. cit.	Green or brown colour before adding H_2O_2 — i.e., neg.	Green or brown precipitate on adding the reagent. Neg. on adding H_2O_2	All negative—agreeing with Ogilvie (1927)	All negative. All clouds white
(*b*) 1/1,000 copper sulphate solution (as copper is contained in some iron preparations)	Negative	Pale green colour. Possible false pos.	Positive — agreeing with Kastle (1909)	Negative	Negative
(*c*) 50 mg./100 ml. ascorbic acid solution	,,	Negative	Negative	,,	,,
(Not confirming the finding of Barrett (1936). The presence of ascorbic acid inhibits all these reactions)					
(*d*) Enzymes: Soya bean 0·5 g. in 5 ml. distilled water. Urease tablets: 1 tablet in 5 ml. distilled H_2O_2	Cold: positive After boiling: negative	Positive Negative	Positive Negative	Negative ,,	Negative ,,
The importance of false positives from enzymes is illustrated by six faecal specimens which, though positive to the benzidine and phenolphthalin reagents in the cold, became negative after boiling					
(*e*) Cold tap-water (Dundee supply) in chemically clean glassware	Negative	Negative	Positive	Negative	Negative
Warm water is even more positive to the phenolphthalin reagent and may give a false positive result with the benzidine test					

(2) Tests of various portions of the same stool were made.
(*a*) Benzidine test on stools of patients on ordinary hospital diet. Five specimens were obtained from each of six stools.

4	stools:	5	specimens positive,	none	negative
1	,,	3	,, ,,	2	,,
1	,,	1	,, ,,	4	,,

(*b*) Modified benzidine test after releasing 2 ml. of blood into the stomach. Five specimens were obtained from each of six stools.

4	stools:	5	specimens positive,	none	negative
1	,,	4	,, ,,	1	,,
1	,,	3	,, ,,	2	,,

If the possibility of alimentary bleeding in small quantities is present one negative faecal occult blood test is quite insufficient to exclude it. Repeated testing is essential.

III. Effects of Diet and Laxatives

The results shown in Table II were obtained by testing faeces not expected to contain blood, obtained from patients eating an ordinary hospital diet including an average amount of meat.

TABLE II

Test	No. of Stools Tested	Positive	Percentage	Results of Bell (1923)
Guaiac	50	19	38	25%
Benzidine, 3 drops	75	59	78·7	70%
,, 10 ,,	150	131 (see Note A)	87·3	
Phenolphthalin ..	75	67 (see Note A)	89·3	58·3%
Gregersen's ..	50*	4 (see Note B)	8	
Modified benzidine	50*	3 (see Note C)	6	
	300	0	0	

* Same specimens.

Note A.—In three patients the stools were often negative to repeated benzidine and phenolphthalin tests: (i) 7 stools tested, 3 positive; (ii) 5 stools tested, 2 positive; (iii) 4 stools tested, 2 positive. A daily laxative was prescribed and the stools were collected again: (i) 4 stools tested, 4 positive; (ii) 3 stools tested, 3 positive; (iii) 5 stools tested, 5 positive. These results conform with the findings of Kirschen *et al.* (1942), who, when testing for the presence of blood in the stools, found purgation to facilitate its detection.

Note B.—One positive result was obtained by Gregersen's method for which no explanation was found.

(2) C.D. had an old infective arthritis of the left hip and had been admitted following right-sided hemiplegia. She died seven weeks after the first positive faecal occult blood test had been obtained. It was persistently positive, but in spite of this Hb was 84% and red blood cells 4,100,000. Post-mortem examination revealed a congenital diverticulum of the second part of the duodenum. It contained the crown of a canine tooth and a spicule of bone. Total dental extraction had been carried out 15 years before.

(3) A boy aged 13 was in hospital for operative correction of strabismus. The positive stool was obtained on the day following operation, at which an endotracheal tube had been passed. This may have accounted for the positive faecal occult blood test.

IV. Sensitivity of Modified Benzidine Test Investigated by Releasing Known Quantities of Blood into Alimentary Tract

(a) *1 ml. of Blood Released into Stomach.*—Initially, the blood was introduced through a Ryle's tube. Faecal occult blood continued to be present for four days in Patient 2; as the test became negative on the fifth day and no other cause for bleeding was found, the results obtained were presumed to have followed trauma by the Ryle's tube. Thereafter the blood was introduced in barium-containing gelatin capsules, which were observed on a fluoroscope to disintegrate in the stomach. No purgatives were given. Discarding Patient 2, the test was positive in only three out of eight patients (Table III). The test is therefore not capable of detecting the presence of blood in the stool following release of 1 ml. in the stomach.

(b) *2 ml. of Blood Released into Stomach.*—In all cases the blood was given in capsules. Apart from Patient 2,

TABLE III

Patient	Day						
	D−2	D−1	D*	D+1	D+2	D+3	D+4
1	−	−	−	−	+	−	−
2	−	−	−	+	+	+	+
3		−	−	−	+	−	−
4	−	−	−		−		−
5	−	−	−	−	−	−	−
6		−	−	−		−	−
7		−	−	−	+	−	
8	−		−		−	−	
9	−		−		−		

* Blood given at 8 p.m., after test.

who was constipated, and from whom no specimen was obtained for four days after the blood was given, the test was positive in all cases (Table IV).

TABLE IV

Patient	Day						
	D−2	D−1	D*	D+1	D+2	D+3	D+4
1		−		−	+	−	
2		−					−
3		−	−	+	−	−	
4		−	−	−	+	−	
5		−	−		+	−	
6		−	−	−	+	−	
7	−		−		+		−
8	−	−			+		−
9	−		−		+	−	

* Blood given at 8 p.m., after test.

(c) *1 ml. of Blood Released into Small Intestine.*—1 ml. of blood was intimately mixed with barium powder and the resulting paste introduced into gelatin capsules—about six to seven capsules for each millilitre of blood. The capsules were then immersed for five minutes in 40% formalin solution and dried. After being swallowed they were observed by fluoroscopy until disintegration occurred—in all cases within one hour of leaving the stomach, the site varying from the duodenum to the small intestine in the pelvis. The test was positive in all cases (Table V).

TABLE V

Patient	Day						
	D−2	D−1	D*	D+1	D+2	D+3	D+4
1	−	−	−	+	−		
2	−		−	+	−		
3	−	−	−	+		−	
4		−	−		+	−	
5		−		+		−	
6	−		−		+		−
7	−	−		+	−		
8	−		−	+	−		
9	−		−		+	−	

* Blood given at 8 p.m., after test.

V. Effects upon Benzidine (B) and Modified Benzidine (M) Tests and upon Colour of Stools following Introduction of Various Quantities of Blood into Stomach by Ryle's Tube

The persistence of blood in the stool following a single haemorrhage into the alimentary tract increases with the amount of the bleeding. Considerable delay occurs before cessation of bleeding becomes evident by negative faecal occult blood tests. In Patient 3 the benzidine test was positive for one day longer than the modified test (Table VI). In all other cases both tests became negative on the same day. Bleeding of more than 100 ml. into the stomach is necessary to produce black stools.

TABLE VI

Patient	Amount of Blood	Test	Day								Colour of Stools
			D −2	D −1	D*	D +1	D +2	D +3	D +4	D +5	
1	10 ml.	B	−	−	−	+	−	−			All normal
		M	−	−	−	+	−	−			
2	20 ,,	B		−	−	+	−		−		,, ,,
		M		−	−	+	−		−		
3	20 ,,	B		−		+	+	−	−		,, ,,
		M		−		+	−	−	−		
4	50 ,,	B		−	−	+	+	−	−		,, ,,
		M		−	−	+	+	−	−		
5	100 ,,	B	−	−	−		+		+	−	Dark brown on D+2 and D+4
		M	−	−	−		+		+	−	
6	200 ,,	B		−	−	+	+		+	−	Black on D+2 and D+4
		M		−	−	+	+		+	−	

* Blood given at 8 a.m., before test.

VI. Effect of above Procedure on Blood-urea Levels

TABLE VII

Patient	Amount of Blood	Blood Urea (mg./100 ml.)			
		D−1 at 11.30 a.m.	D at 11.30 a.m.*	D at 3.30 p.m.	D+1 at 11.30 a.m.
3	20 ml.	27	33	30	
4	50 ,,	28	49	39	30
5	100 ,,	25	28	30	24
6	200 ,,	28	43	40	37

* Blood given at 8 a.m.

In the presence of bleeding into the alimentary tract the normal level of blood urea would not be known. When such conditions are applied to the experiment the maximum figures obtained are not high enough to be considered significant (Table VII). Such factors as dehydration, impaired clearance of urea, increased breakdown of tissue proteins, and diminished fluid intake have been shown by Black (1940) to contribute to the raised blood-urea level following gastro-duodenal haemorrhage. It is unlikely that these effects would be brought into play after haemorrhage in the amounts imitated experimentally here, so that any rise in blood urea would be the result of increased absorption of nitrogen from the blood in the bowel. In bleeding of this degree, therefore, the stools become black before a significant rise occurs in the blood-urea level.

VII. Benzidine and Modified Benzidine Tests in Presence of Pathological Bleeding into Alimentary Canal

Faecal occult blood was presumed to be present when the benzidine test remained positive after four days on a haemoglobin- and chlorophyll-free diet. In groups 1, 2, and 3 (Table VIII) both tests became negative on the same

TABLE VIII

Disease	No. of Cases	
	Positive Benzidine Test	Positive Modified Benzidine Test
1. Bleeding peptic ulcer	3	3
2. Melaena from duodenal ulcer	1	1
3. Haematemesis from peptic ulcer	4	4
4. Bleeding gastric neoplasm	9	9
5. ,, colonic ,,	4	4
6. ,, caecal ,,	5	5
7. Polyposis coli	1	1
8. Thyroid carcinoma invading oesophagus	1	1
9. Duodenal diverticulum	1	1
10. Strangulated inguinal hernia (not on Hb-free diet)		1
11. Bacterial endocarditis with emboli	1	1
12. Chorea	2	2
13. Pulmonary tuberculosis with blood-stained sputum	1	1
14. Following haemoptysis (unexplained)	1	1
	34	35

day, except in one case of bleeding peptic ulcer, in which the benzidine test was positive for one day longer than the modified test. In this very small series the modified test has not failed to reveal the presence of blood in the stools.

Discussion

Tests for occult blood in faeces are expected to provide information about the presence of a lesion in the alimentary tract, and the time when bleeding, already known to be present, ceases. How well do they succeed?

A negative faecal occult blood test does not imply the absence of a lesion in the alimentary canal. All ulcers and neoplasms do not bleed all the time. The paper of Dahl-Iversen and Nissen (1930) giving the percentage of positive tests in the presence of intestinal neoplasms as 92.5 merely illustrates that 7.5% of such tumours were not bleeding at the time of testing, or at least that the particular portions of faeces tested did not contain blood. Such evidence does not allow a conclusion that the tests are of insufficient sensi-

tivity. Abrahams (1923) and Bell (1923) both showed that 1 ml. of blood introduced into the stomach resulted in positive guaiac and benzidine reactions. As this 1 ml. of blood was contained in the daily stool it is evident that the tests are capable of detecting bleeding into the stomach of the order of 1 ml. in 24 hours. The phenolphthalin test is even more sensitive. The modified benzidine test described here (and probably the equally sensitive Gregersen's test) will become positive following the release of 2 ml. of blood in the stomach or 1 ml. in the small intestine—that is, it is capable of detecting bleeding in these amounts in 24 hours. As shown by two cases described in III (Note C), such a loss of blood would be insufficient to bring about a state of anaemia. III (Note A) illustrated how delayed passage through the gastro-intestinal tract tends to result in failure to detect blood in faeces; while II (1) indicates that a negative result from one specimen, however sensitive the test, does not exclude the presence of blood from the whole stool. Therefore, a negative result from a faecal occult blood test cannot, without considerable care, be taken to indicate the absence of bleeding. The significance of a negative test is thereby much diminished.

A positive faecal occult blood test, in the absence of any known pathological condition, is the signal for a series of endoscopic, radiological, bacteriological, and, maybe, haematological investigations to find the cause of bleeding. Occasionally all these measures prove fruitless, whilst blood remains present in the faeces. In such an event laparotomy may be resorted to as the final diagnostic measure. Failure of barium examinations, both meals and enemata, to reveal neoplasms of the colon, and especially of the caecum, is not an uncommon experience. The particular importance of a positive faecal occult blood test is therefore clear. It is equally important that no test should be positive in the absence of pathological bleeding.

Unfortunately, the more sensitive the test to the presence of blood the more likely is it to yield false-positive results. Dietary restriction must be strict and absolutely reliable before a positive guaiac, benzidine, or phenolphthalin test is accepted as indicating the presence of blood. The sensitivity of these tests requires that bleeding in excess of 0.5 to 1 ml. in 24 hours from gum-sucking or tooth-brushing be excluded (not to mention haemorrhoids). Although too vigorous tooth-brushing may be prevented, it is quite impossible to avoid nocturnal tooth-grinding—a not uncommon habit and one apt to cause bleeding. Saliva was obtained on awakening from two children and an adult—all confirmed tooth-grinders—and, after boiling, was tested with the benzidine reagent. All three tests were positive, whereas normal boiled saliva gives a negative result. Ogilvie (1927) found the relatively insensitive Gregersen test to be positive in cases of rheumatic fever and chorea as a result of bleeding from the gums. Gurling (1951), using the benzidine test, found no explanation for 10% of 117 positives obtained by him out of 316 tests—a high figure which detracts markedly from the clinical significance of a positive result. Such observations apply in even greater measure to the more sensitive phenolphthalin test, and, conversely, in lesser degree to the guaiac reagent.

The main objection to Gregersen's test—and hence to the modified benzidine test which is described here—is its lack of sensitivity. It is undoubtedly possible for both tests to fail to reveal minute quantities of blood in faeces detectable by tests of greater sensitivity. It has been shown here that in one patient given 20 ml. of blood into the stomach, and in another bleeding from a peptic ulcer, the benzidine test remained positive for one day longer than the modified test. But how important is this lack of sensitivity from a clinical point of view? It may be categorically stated that should a patient suffer from anaemia secondary to alimentary bleeding the presence of blood in the stools will be detected by the modified test. So far as the early diagnosis of gastro-intestinal conditions is concerned, does it really matter whether bleeding is detected in amounts less than 1 or 2 ml. in 24 hours? In view of the fallacies attendant upon extreme sensitivity noted above, it is doubtful whether the presence in faeces of such minute amounts of blood may be affirmed with any confidence in those cases in which a positive faecal occult blood test is the only positive finding. The particular test's sensitivity is surely outweighed by the importance of repeated and frequent testing (II, 2) facilitated by the less sensitive tests, easy as they are to perform and requiring no dietary restriction. In addition it is highly improbable that such small differences in bleeding are related in any way to the operability of a neoplasm. Furthermore, bearing in mind the considerable delay between cessation of bleeding and faecal blood tests becoming negative (see V), the knowledge that the 24-hour blood loss has fallen below 1 ml., as distinct from 2 ml., is valueless. Such pursuit of perfection ruins the clinical value of faecal occult blood tests.

The desirability of reducing the sensitivity of both benzidine and phenolphthalin tests has been recognized. To this end the "ring" method of using the benzidine reagent was introduced—that is, pouring the hydrogen peroxide down the side of the tube without shaking and awaiting the appearance of a blue ring at the fluid junction. However, dietary restriction is still necessary (Bell, 1923). With the phenolphthalin test it is said that a red colour appearing within 20 seconds *only* should be regarded as positive: the variable sensitivity of the reagent makes the discarding of a colour appearing in 21 seconds an act of great faith. Similarly, the time limit necessary in Gregersen's method is an encumbrance, for it is difficult not to notice a blue colour appearing a few seconds late.

The modified benzidine test is suggested for adoption for these reasons: the reagent is easy to prepare in constant composition; the test is easy to perform; it does not give false-positive results from the presence of enzymes or ingested blood; it does not require timing; and in this small series of cases of pathological bleeding into the alimentary tract it has not failed to reveal the presence of blood in the faeces. It is fully realized that its value has yet to be determined by trial in large numbers of cases, although, as the sensitivity of both tests is identical, it should be as successful in detecting blood as Gregersen's modification.

Summary

The sensitivity of the guaiacum, benzidine, phenolphthalin, Gregersen's, and the simplified benzidine tests are compared, using serial blood dilutions.

Possible fallacies in testing faeces for blood are examined. It is shown by testing various portions of the same stool that some tests may be negative even in the presence of blood.

The effects of diet and laxatives on the tests are described, and two cases giving unexpectedly positive results are quoted. These illustrate that the simplified benzidine test will detect bleeding before secondary anaemia becomes evident.

The sensitivity of the simplified benzidine test is such that it will detect 2 ml. of blood released into the stomach or 1 ml. released into the small intestine.

Following release of varying quantities of blood into the stomach, it is shown that more than 100 ml. is necessary to produce black stools; that the stools become black before a significant rise in blood urea occurs; and that much delay elapses before cessation of bleeding becomes manifested by negative faecal blood tests.

In a small series of 35 cases the simplified benzidine test has not failed to detect pathological bleeding into the alimentary canal.

The value of tests of greater or lesser sensitivity is discussed from the point of view of clinical diagnosis.

Nocturnal tooth-grinding is shown to be a cause of bleeding into the mouth. Tests of lesser sensitivity are recommended.

The advantages of the newly introduced simplified benzidine test are enumerated.

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TRANSFUSION TREATMENT OF WOMEN OF CHILD-BEARING AGE

A STATISTICAL STUDY OF THE INCIDENCE OF ANTI-RHESUS IMMUNIZATION

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The increased use of blood transfusion in the treatment of a great number of conditions has brought into the foreground complications which in the past must have been more or less rarities. The immediate effects of transfusion in saving the lives of many patients has on certain occasions been followed by the production of antibodies. Some of these antibodies may play a decided part in the future life of the patient. Serologically the great majority of the antigens carried on or in the red cells of man seem to be poor antigens, but even poor antigens will produce antibodies in "good reactors," particularly if given in sufficient quantity.

By far the most important antigen of the cells in this respect—apart from the antigen responsible for the ABO specificity—is the rhesus antigen. Compared with other blood-group antigens it provides a comparatively potent stimulus for antibody production, and is thus capable of immunizing an appreciable percentage of patients lacking the antigen themselves. Diamond (1946) has shown, in an investigation performed on war veterans, that approximately 46% of rhesus-negative men who were transfused in the field were found to be immunized against the rhesus factor. The blood given in most of these emergencies was presumably rhesus-positive blood. Although the production of antibodies in the male might have serious consequences if the patient should later require a further transfusion, the sequelae in the female are far more serious, since the presence of antibodies may, under certain circumstances, prevent her from ever having a healthy child. Among the mothers who bore children affected with haemolytic disease of the newborn are a certain number whose immunization had either been started or been greatly stimulated by one or more previous transfusions of rhesus-positive blood. The percentage of immunized women is very much higher among those who have received a previous transfusion than among those who were not so treated. The growing knowledge of the dangers of immunization by transfusion has, generally speaking, resulted in an improved technique and fewer cases of immunization. This investigation was undertaken in order to find out whether the number of patients whose immunization has been precipitated by transfusion treatment in the past has declined lately.

Material and Methods

The material has been taken from the Regional Transfusion Service, Birmingham, and consists of the records of approximately 82,000 patients whose blood samples were investigated up to the end of 1949. This investigation consisted always in the determination of the group and the rhesus type of the patient. In all cases which were found to be rhesus-negative an investigation for the presence of antibodies was performed routinely. For the latter investigation the following method was used. Eight random samples of rhesus-positive saline-suspended cells and two samples of rhesus-positive and two of rhesus-negative albumin-suspended cells were put up in precipitin tubes as recommended by the Medical Research Council (1943). An equal amount of the patient's serum was then added to the test cells and the mixture was incubated at 37° C. for two hours. The tests were always read under the low power of the microscope on a slide. If in this screening test agglutination was found in either the saline- or the albumin-suspended test-sample cells, a fuller investigation was carried out.

This same fuller investigation was also done if the history of the patient indicated immunization or if a transfusion had been given at some time previously in her life. The method used was as follows. The serum of the patient was put up with ten random rhesus-positive and two random rhesus-negative saline-suspended cells. The same cells were used as test cells in albumin suspension and simultaneously incubated with the saline-suspended cells (incubation two hours at least). Indirect Coombs tests, using CDe, cDE, and cde cells, were also performed with every sample.

All the patients in whose sera antibodies were discovered were followed up by frequent investigations until delivery. In most cases the diagnosis was confirmed either by the result of the pregnancy (hydrops) and/or a Coombs test on the baby's blood. In many cases a sample of blood taken from the husband was investigated for its genotype. The clinical data concerning the patients were obtained from the medical officers in charge of the hospitals and antenatal clinics on the usual antenatal forms. Further information was obtained in special cases. The data were transferred to a filing-card, on to which were entered also the result of the serological investigation and any subsequent development. The cases were arranged according to the date on

which the transfusion had taken place. Arbitrarily the date of December, 1947, was taken as a dividing-line. This date was chosen because at this time, approximately, the knowledge of the dangers of non-homologous transfusions became more widespread and the supply of rhesus-negative blood of all groups had become somewhat more plentiful by a revised bleeding programme.

Results

Among approximately 82,000 cases investigated up to the end of 1949 were found 13,169 patients who were rhesus-negative. Of the latter, 515 (3.9%) were found to be immunized against the rhesus factor (D). Among the total of 13,169 patients investigated, 243 gave a history of having received a blood transfusion at some time during their lives or blood injections of untyped blood which was given as a therapeutic measure. It is possible that the number of women who, as girls or babies, had received blood injections is greater than the actual number found among our patients, as these data depend very often only on the recollection of their parents, who might not have informed their children. Of the 243 patients who had been treated with blood transfusion or injections, 87 were found to be immunized against the rhesus factor. This leaves 428 who, with no history of a previous transfusion, were found to be immunized.

Before 1947 many patients will have received, particularly in emergencies, transfusions of untyped or rhesus-positive blood. The chance of a rhesus-negative patient receiving initially 1 pint (570 ml.) of rhesus-positive blood is about 85 in 100, but the chance of receiving at least 1 pint (570 ml.) of rhesus-positive blood increases with successive transfusions (second, 977 in 1,000; third, 997 in 1,000). As pointed out above, both the knowledge of the dangers of immunization and the availability of rhesus-negative blood increased after 1947. In the Birmingham Blood Transfusion Centre the average monthly number of blood samples from pregnant women which were investigated for the rhesus factor ("D screening") increased as follows:

Second half of 1947	2,334	Second half of 1949	5,869
First " " 1948	3,340	First " " 1950	6,306
Second " " 1948	4,469	Second " " 1950	6,015
First " " 1949	5,700	First " " 1951	6,602

The numbers of pints of rhesus-negative blood issued annually were as follows: in 1947, 1,551; in 1948, 2,447; in 1949, 4,953; and in 1950, 6,824.

Table I sets out in detail the occurrences of immunization among transfused persons. It will be seen that in most of the years previous to 1947 over 40% of the transfused

TABLE I.—*Immunization Among Transfused Persons*

	'40*	'41	'42	'43	'44	'45	'46	'47	'48	'49	Total
Primigravidae transfused and immunized	2		1				1		1	1	6
Multigravidae transfused and immunized	10	2	4	6	8	12	15	12	10	2	81
Primigravidae transfused and *not* immunized	1		2	1	1	2	3	4	3	12	29
Multigravidae transfused and *not* immunized	13	4	7	7	8	8	17	24	26	13	127
Total	26	6	14	14	17	22	36	40	40	28	243
Percentage of immunized women	46	33	36	43	47	54	44	30	27	11	36

* Includes some cases that occurred before 1940.

rhesus-negative women were immunized. The percentage declined in 1947 and 1948, and in 1949 it was much less.

Table II shows the difference of the percentage of immunization among the transfused persons: 41.7% before and including 1947, 20.6% after 1947. The difference of 21.1% has an estimated standard deviation of 6.8%; thus the probability of so large a difference occurring by chance is about 1 in 500. In the second part of this table a comparison is

TABLE II.—*Immunization Among Transfused Rhesus-negative Women*

Period	Total No. of Transfused Women	% Immunized	Difference %	Estimated Standard Deviation %	P
Transfusions: 1940–7	175	41·7	21·1	6·8	0·002
Transfusions: 1948–9	68	20·6			
Transfusions: 1944–7	115	41·7	21·1	7·3	<0·003
Transfusions: 1948–9	68	20·6			

made between transfusions known to have taken place in the period 1944 to 1947 and those in 1948–9. The difference is 21.1%, its estimated standard deviation 7.3%, and the probability of such a difference occurring by chance is less than 1 in 100.

In Table III the incidence of immunized persons in two-year groups, up to and including 1947, is compared with that in the period 1948–9. In each case the difference is too large

TABLE III

Period	No. of Transfused Women	% Immunized	Difference %	Estimated Standard Deviation %	P
1940–1	32	43·7	23·1	9·6	0·016
1948–9	68	20·6			
1942–3	28	39·3	18·7	9·8	0·057
1948–9	68	20·6			
1944–5	39	51·3	30·7	9·4	0·001
1948–9	68	20·6			
1946–7	76	36·8	16·2	7·6	0·036
1948–9	68	20·6			
1944–5	39	51·3	14·5	9·7	0·134
1946–7	76	36 8			

to be regarded as a chance effect. The period with the highest percentage (1944–5) is compared with that having the lowest percentage (1946–7), 1948–9 being excluded. The difference of 14.5% is probably due to chance, since it might be elicited 13 times out of 100.

Table IV shows the actual and expected numbers of immunized women up to the end of 1947. There is little dif-

TABLE IV

Period	No. of Transfusions: With Immunization Actual	With Immunization Expected	Without Immunization Actual	Without Immunization Expected	Total
1940–1	14	13·35	18	18·65	32
1942–3	11	11·68	17	16·32	28
1944–5	20	16·27	19	22·73	39
1946–7	28	31·71	48	44·29	76
Total	73	73·01	102	101·99	175

$\chi^2 = 2{\cdot}327$. $0{\cdot}70 > P > 0{\cdot}50$.

ference between the actual and the expected numbers, since they may occur by chance about seven times out of ten.

Table V shows the actual and expected numbers when the period 1948–9 is included. In this case the actual number

TABLE V

Period	No. of Transfusions: With Immunization Actual	With Immunization Expected	Without Immunization Actual	Without Immunization Expected	Total
1940–1	14	11·46	18	20·54	32
1942–3	11	10·02	17	17·98	28
1944–5	20	13·96	19	25·04	39
1946–7	28	27·21	48	48·79	76
1948–9	14	24·34	54	43·66	68
Total	87	86·99	156	156·01	243

$\chi^2 = 11{\cdot}98$. $P = 0{\cdot}02$.

of cases is less than the expected number in the last period only (1948–9); the actual number exceeds the expected in each of the other periods. The probability of this difference being due to chance is only 1 in 50.

From the above it seems to be quite clear that the number of women immunized by a transfusion was greater before the end of 1947 than after this period. With and without transfusion, a certain number of rhesus-negative mothers are bound to become immunized if the foetus is rhesus-positive, but the figures will be much higher if precautions are not taken to prevent artificial immunization by transfusion in the rhesus-negative population.

Discussion

Though the figures show a definite improvement in the two years under review as compared with previous years, they seem to be still too high to be accepted with complacency. It would appear to be imperative to adopt effective measures to reduce these figures still further, and no case of immunization by transfusion in a female should ever occur. As the great majority of transfusions are "cold" transfusions there is usually enough time to group and type the patient so that homologous blood can be given. Most hospitals have by now a blood bank run by the pathological laboratory; blood grouping and typing has reached in most parts of the country a very high standard indeed, and technical mistakes are very rare.

With regard to emergency transfusions, a simple procedure would serve to prevent immunization and at the same time save the rare rhesus-negative blood, particularly of Group O: a female patient admitted in an emergency is treated, to start with, as if she was rhesus-negative, and rhesus-negative blood is given. If the group is known or if there is enough time at least to determine the group, rhesus-negative blood of the same ABO group may be given if available. Before the transfusion is begun an adequate sample of blood from the patient is put into a test-tube and sent immediately to the laboratory, where grouping, typing, and cross-matching can be performed. If further blood is needed for the patient, this can then be given as homologous blood, and rhesus-positive patients will receive positive blood. The great amount of antenatal care and the issue of grouping cards by the transfusion centres have further increased the safety of transfusion treatment. The flying squad, for instance, in Birmingham during 1946 and 1947 was issued with rhesus-negative blood only. Lately it has been found possible to make use of rhesus-positive blood, as many emergency patients can now produce their blood-grouping cards on request. If the patient has been typed as rhesus-positive, homologous rhesus-positive blood is given.

The scarcity of anti-rhesus serum, which at one time seemed to limit a further expansion of antenatal typing, will, it is hoped, be overcome in the future if pathologists and clinicians realize the importance of its availability and will help to persuade immunized mothers to contribute some serum to the common pool.

Conclusion and Summary

Using the figures obtained from the records of the Regional Transfusion Service in the Midlands, it has been shown that the percentage of immunization among rhesus-negative mothers due to previous transfusions has gone down significantly in the two years 1948 and 1949 as compared with previous periods. It is felt, however, that no immunization should ever occur if simple precautions are taken in the treatment of girls and women of pre-child-bearing or child-bearing age.

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INFECTIOUS MONONUCLEOSIS WITH THROMBOCYTOPENIC PURPURA

BY

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A tendency to abnormal bleeding in patients with infectious mononucleosis has been noted for many years, but a true thrombocytopenic purpura has been recognized only since Magner and Brooks (1942) reported a case. Accounts of nine other cases have now been published, six of these during the past two years. Despite this increased recognition of the condition, only one instance has been reported in the European literature (Finlayson, 1951) Thrombocytopenia is not mentioned in many recent accounts of infectious mononucleosis published in this country, but it is still quoted as diagnostic evidence of acute leukaemia in the differentiation of this condition from infectious mononucleosis. We describe a further case of thrombocytopenic purpura in infectious mononucleosis and review the literature on this complication.

Case Report

An unmarried girl aged 20 was admitted to the Liverpool Royal Infirmary as a case of purpura on May 11, 1951. She complained of lassitude, sore throat, swollen glands, and a rash on her arms and chest. Her previous health had always been good, and neither the patient nor her family had ever shown abnormal bleeding tendencies. She had not recently taken drugs in any form and was not exposed to toxic substances at her work.

On admission she stated that she had felt tired and "run-down" for about a month but had remained at work. For the same period she had been aware of enlarged glands behind her right ear; these had not altered in size. Three days before admission red spots appeared over the neck, the upper part of the chest, the upper arms, and the radial border of the left forearm. This rash developed in about 48 hours and gradually faded during the ensuing fortnight. On the day of admission she complained of sore throat, which remained for about a week. A menstrual period two weeks before the rash appeared was not excessive.

Examination revealed a lively and well-nourished girl showing no pallor or jaundice. Her temperature on three evenings during the first week in hospital was 100–101° F. (37.8–38.3° C.), and thereafter remained normal. Crops of petechiae were found on the left arm and breast, and larger purpuric areas on the right upper arm and left thigh. Hess's test for capillary fragility was negative. Firm, discrete mobile lymph nodes were palpated behind the upper part of the right sternomastoid, and one node was felt in a similar position on the left side. Inguinal and axillary lymph nodes were normal and the spleen was not palpable. The faucial pillars were injected and a mucous exudate partially covered the tonsils, but the mucous membranes were otherwise normal and no haemorrhagic lesions were seen in the mouth. The examination revealed no other abnormal features.

A blood examination on admission showed no anaemia. There were changes in the white cells typical of infectious mononucleosis, and this diagnosis was confirmed by a strongly positive Paul–Bunnell reaction. A platelet count revealed a marked thrombocytopenia (the haematological findings are enumerated in the accompanying table).

TABLE

Date	Haemoglobin %	White Blood Cells per c. mm.	Polymorphs %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Atypical Mononuclears %	Platelets per c.mm.	Bleeding Time (Duke's Method)	Clotting Time (Wright's Method)
11/5/51	100	14,000	13	59	2·5	—	0·5	25	12,000		
16/5/51	—	—	—	—	—	—	—	—	130,000		
21/5/51	—	5,000	27	56	13	1	1	2	350,000	1 min.	3½ min
22/6/51	—	—	—	—	—	—	—	—	270,000		
27/6/51	97	6,000	43	48	8	1	—	—	260,000	1½ min.	
8/1/52	100	7,000	60	33·5	4	1	—	1·5	295,000	2 min.	4½ min

A differential count on a specimen of sternal marrow obtained on May 16 was as follows (400 cells were counted): reticulo-endothelial cells, 0.25% ; blast cells, 0.25% ; haemocytoblasts, 0 ; proerythroblasts, 0.25% ; normoblasts : early 0.75%, intermediate 3.5%, late 20.0% ; megaloblasts, 0 ; promyelocytes, 7.25% ; myelocytes, 4.5% ; eosinophil myelocytes, 0.75% ; metamyelocytes, 18.25% ; eosinophil metamyelocytes, 0.5% ; polymorphs, 6.75% ; lymphocytes, 18.75% ; eosinophils, 0.75% ; basophils, 0 ; monocytes, 9.75% ; plasma cells, 1.75% ; atypical monocytes, 5.0% ; unidentified cells, 1.0%. The myeloid erythroid ratio was 1.5:1. Platelets were very scanty in the marrow films and no megakaryocytes were seen when counting 400 cells. When the films were examined under the ⅓-in. objective, megakaryocytes, although present, were fewer than normal, and while some were normal mature cells others were much smaller with a large kidney-shaped nucleus almost filling the whole cell, and appeared to be young immature forms.

On May 15 the Paul–Bunnell reaction was positive to a titre of 14,000 with both the unabsorbed and the guinea-pig-kidney absorbed serum, but only to 1/28 with the serum absorbed with ox cells. Six weeks later, June 27, the titre was 7,000 and on January 9, 1952, 1/112. The blood Kahn test was negative on June 27, 1951.

Vincent's organisms were not demonstrated in direct smears of throat swabs, and cultures yielded *Neisseria* and *Streptococcus viridans* only. No abnormality was found in the urine. The van den Bergh reaction, the serum alkaline phosphatase, and the flocculation tests for liver function were within normal limits. The chest radiograph was normal.

The patient recovered without treatment and was discharged free from symptoms after 12 days in hospital. The rash disappeared during this time and no fresh petechiae were noted. One month later she reported that several bruises had appeared on her legs. She had otherwise remained well and a menstrual period had been normal. Physical examination was negative, a platelet count was normal, and the blood picture now showed only a slight predominance of lymphocytes. No further symptoms had developed up to the time of writing, and on January 8, 1952, no clinical or haematological abnormality was found.

Review of Literature

Haemorrhage (epistaxis) was observed in a case of infectious mononucleosis in 1895, and many other instances of mucosal bleeding—epistaxis and haematuria especially—have been reported since that time. In 1921 Tidy and Morley found haematuria in 6% of 270 patients, and in 1945 Read and Helwig reported mucosal haemorrhages (from the nose, mouth, or lung) in 4% of their series.

Cutaneous purpura was first reported in a case of infectious mononucleosis by Downey and McKinlay (1923), but Tidy (1934) could find only four other instances in the literature. Bernstein (1940) quoted two further cases, and a third in which infectious mononucleosis had exaggerated a pre-existing haemorrhagic state. Recently, purpura has been reported more often in infectious mononucleosis, but it is not common ; it was found in only 1 of 290 cases reviewed by Halcrow *et al.* (1943), in 9 of Read and Helwig's (1945) series of 300, and in 3 out of 556 cases reported by Wechsler *et al.* (1946). Rosenthal (1939), reviewing the aetiology of 153 cases of purpura, mentions that in four "the picture resembled mononucleosis."

Thrombocytopenia, with or without purpura, would appear from the earlier literature to be a very rare event in infectious mononucleosis. Bernstein (1940) was able to quote four references to thrombocytopenia without purpura, while Minot's (1936) four patients with thrombocytopenic purpura and an "atypical white cell response" were not thought by the author to be cases of infectious mononucleosis. It should be noted, however, that platelet counts are rarely performed in infectious mononucleosis and are even omitted from early accounts of purpura in this condition. In recent years platelet counts have been done more often ; Angle and Alt (1950) found a mild thrombocytopenia (100,000–200,000 per c.mm.) in five out of seven cases of infectious mononucleosis without purpura or haemorrhage, and 10 cases of thrombocytopenic purpura complicating proved infectious mononucleosis have been published since 1942 (Magner and Brooks, 1942 ; Lloyd, 1944 ; Read and Helwig, 1945; Goldbloom and Denton, 1948 ; Angle and Alt, 1950 ; Wallerstein and Madison, 1950 ; Kutzer and Allen, 1950 ; Thompson, 1950 ; Finlayson, 1951).

Except for the various purpuric manifestations, the clinical and pathological findings in these cases are not significantly different from those found in uncomplicated infectious mononucleosis. Haemorrhagic features appeared in each case during the first fortnight of the illness, and subsided within one to four weeks. The purpura was seen most often on the legs, and also occurred in the mouth in the majority of patients. Spontaneous mucosal bleeding was reported in all but two cases, haematuria and epistaxis being the most frequent. When reported, the clotting-time was normal, clot retraction defective, and the bleeding-time and capillary fragility were usually, but not invariably, increased. Anaemia was never present at the onset of the illness, but appeared later in two patients. (The case reported by Read and Helwig was unusual in that there was a progressive fall in the red cells, white cells, and platelets, followed by a gradual return to normal.) The platelet count fell to below 100,000 per c.mm. in every case, and in five patients did not return to a normal level for more than six weeks ; the severity of the haemorrhage could not be correlated with the number of circulating platelets. The bone marrow was examined in five cases, and in two the megakaryocytes were reduced in number. All the patients made a complete clinical and haematological recovery ; only two were regarded as seriously ill and two required blood transfusions. Death due to a ruptured spleen has been recorded in a similar case by Smith and Custer (1946), but the Paul–Bunnell reaction in this patient was negative.

Comment

Various explanations of this rare complication of infectious mononucleosis have been offered. Bethell *et al.* (1946) suggested that a sulphonamide drug might be responsible in some cases, but in fact only two of the patients in this series were given a sulphonamide. Read and Helwig postulated an infective granulomatous infiltration of the bone marrow, but their case showed anaemia and leucopenia as well as a fall in platelets. Lloyd (1944) attributed the purpura to

an acute infection leading to capillary damage with loss of circulating platelets at the purpuric sites. In other acute infective conditions with purpura, however, the patient is usually gravely ill. Several of the authors quote Dameshek and Grassi's (1946) case, in which there was a dramatic response to splenectomy, and attribute the purpura to hypersplenism. Although this theory may be correct, it should be noted that Dameshek and Grassi's patient had suffered from a haemorrhagic condition for two years before it was aggravated by infectious mononucleosis, and is thus not strictly comparable to the cases under discussion. Whereas the spleen was "considerably enlarged" in Dameshek and Grassi's case, it was not palpable in half the patients in this series, and in the remainder it was only slightly enlarged.

Lymphatic hyperplasia seems to be a factor common to a number of cases of thrombocytopenic purpura in which no other cause for the platelet reduction has been found (Minot, 1936; Cooley, 1938; Lytle and Ward, 1937). In Cooley's patient, for example, greatly enlarged abdominal lymph nodes were found at necropsy. He remarked upon the identical microscopical appearances of the lymph nodes and spleen, and thought that the lymph nodes were taking part with the spleen in platelet destruction. In the case of infectious mononucleosis which we have reported the immediate cause of the thrombocytopenia appeared to be a deficiency of the megakaryocytes in the bone marrow; this finding was also recorded by Wallerstein and Madison (1950).

Conclusion

We would suggest that in patients presenting with purpura, especially children and young adults, infectious mononucleosis should be excluded by means of the Paul–Bunnell reaction. A wrong diagnosis of acute leukaemia or "essential thrombocytopenia" may otherwise be made, and this may lead in the first case to the neglect of life-saving measures and in the second to unnecessary splenectomy. The absence of anaemia at the onset of the purpuric phase is a constant finding in infectious mononucleosis, and will help to exclude acute leukaemia.

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In a recent address on "Diagnosis in General Practice" the retiring president of the Royal Society of Medicine's Section of General Practice, Dr. J. D. Simpson, divided patients into four classes, depending on their doctors' knowledge of the patient himself, the pathological process, and the patient's environment. His classification was as follows: (1) the old patient with the old disease, where all three were known; (2) the old patient with the new disease, where a pathological process had to be assessed afresh; (3) the new patient with the old disease, where history or previous doctor's notes might help; and (4) the new patient with the new disease.

Medical Memorandum

Use of the Humby Knife in the Excision of Burns

The importance of early excision of the extensive deep burn has become recognized in recent years. The surgical removal of these large full-thickness sloughs may offer the only chance of survival in those once-hopeless cases which, thanks to improved methods of controlled intravenous-fluid therapy, are now being brought through the shock phase in increasing numbers. It is a tedious and time-consuming operation, however, and is often accompanied by considerable blood loss, although this factor may be minimized by the use of methonium drugs in carefully selected cases.

A recent improvement in technique has been found so helpful in this unit that it appeared to warrant publication of this short note.

Case 1

A female patient aged 38 had suffered severe deep burns involving 60% of her body surface. She was treated by the exposure method, and on the eleventh day after burning was taken to the theatre for excision and grafting, partly with homografts and partly with her own available skin. In an endeavour to reduce operating time a Humby knife was applied to an extensive slough on the upper part of the back. This was removed with such ease and rapidity that the remaining areas were dealt with in the same manner (see illustration).

Case 2

A few days later the technique was employed in the case of a female epileptic aged 29 who had sustained a deep "roasting" burn of the trunk and other areas, totalling 32% of the body surface. Excision was performed on the seventh day after burning, autografts being applied and the procedure completed in three-quarters of an hour. In this case a considerable depth of fat was found to be non-viable, and in certain areas it was necessary to remove it in two layers.

Comment

The Humby knife used in this procedure is the familiar graft-cutting instrument consisting of a long blade the cutting edge of which is guarded by a roller adjustable according to the depth of skin required. The knife is set to cut more deeply than for ordinary use, and preliminary scalpel punctures of the slough may assist in giving some idea of the required depth. It is difficult to describe the ease and selectivity with which these adherent sloughs are removed at the correct level and the manner in which it is possible to follow difficult contours without damage to neighbouring intact skin. Blood loss is minimal, and an even surface is left which is ready for immediate skin-cover. This technique is now being employed in most cases of severe deep burns, and, together with the use of the electric dermatome, is making excision and grafting at an earlier stage a much more practical proposition.

I wish to thank Sir Harold Gillies for permission to publish this short memorandum.

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Reviews

REFRESHER COURSE

Refresher Course for General Practitioners: specially commissioned articles from the *British Medical Journal*. First collection: October, 1949, to December, 1950. (Pp. 502. £1 5s.) London: B.M.A. 1952.

In this volume are collected 55 articles, which first appeared in this *Journal*, written by experts on subjects of interest to the general practitioner. With so much knowledge surging round him the general practitioner needs to keep his balance. Chapters by Professor Garrod (penicillin, streptomycin, and the newer antibiotics) and by Professor Dunlop (sulphonamide therapy) are excellent examples of well-balanced information. Sir Charles Symonds (management of the epileptic) and Professor Platt (hypertension) are teachers at whose feet it is a privilege to sit. They take care to explain why they believe what they believe. Authority without dogma, erudition with common sense, are also notable in short articles by Dr. Philip Evans (infant feeding), Dr. Macdonald Critchley (migraine), and Mr. Zachary Cope (acute abdominal disease). There are two little gems on fractures of the clavicle and scaphoid by the late Professor McMurray and by Professor George Perkins. Many will enjoy the imaginative flights of Dr. Cyriax (treatment of lumbar disk lesions).

Dogmatic teaching may be convenient but is liable to pitfalls. For examples, Mr. Theobald (post-partum haemorrhage) apparently believes insomnia to be a cause of insanity, whereas the converse is more likely true. Dr. Langton Hewer (analgesia in childbirth) states that babies benefit from painless birth, but gives no evidence. Mr. Stallworthy (menorrhagia), after lecturing the general practitioner on the distinction between *post hoc* and *propter hoc*, gives constipation as a cause of menorrhagia. On the other hand Dr. Bishop (menstrual disorders and the menopause) writes a lucid account of modern theories on the endocrinology of the ovary.

As well as being instructed the general practitioner will be inspired by reading Dr. MacKenna on psoriasis, Professor Craig on pink disease, and Dr. Beaumont on the treatment of ulcerative colitis. The persistence, patience, and care as well as skill of first-rate physicians hold many lessons for the general practitioner in these hurried times.

The articles on tuberculosis—diagnosis of early phthisis, early diagnosis of tuberculous meningitis, and management of pulmonary tuberculosis—seem to lack perspective. For one thing the early diagnosis of well-established disease is a very limited objective. Secondly, the role of the general practitioner is uncertain; but surely it will not in the future depend on his clinical acumen or lucky guessing. The older general practitioner may find Dr. Black (modern views on uraemia and dehydration) and Dr. East (electrocardiography) fairly hard on the teeth, but he will be relieved to read that out of the present complexity a clearer simplicity will emerge.

Whether he wishes to learn, to admire, or to argue, this volume will open many windows in the general practitioner's mind, windows which may have long been closed. The book is well printed and beautifully illustrated, for the most part by Miss Sylvia Treadgold.

C. W. WALKER.

QUICK REVISION

A Handbook of Surgery. By Reginald C. B. Ledlie, M.B., B.S.(Lond.), F.R.C.S., and Michael Harmer, M.B., B.Chir. (Cantab.), F.R.C.S. (Pp. 536; 56 figures. £1 1s.) London: Baillière, Tindall and Cox. 1951.

On the jacket of this book the reason for its publication is explained thus: "Many of the standard textbooks have expanded so largely that the need of a book expounding adequately yet concisely the art and practice of surgery had become evident. With this in mind the authors have deliberately limited the volume to a little over 500 pages, and have presented the subject matter in a convenient form both for a ready grasp of essentials and for easy revision and reference." The book is therefore a summary, almost an epitome of summaries, and as such it must be regarded as a satisfactory production. Indeed, the authors are to be congratulated on having achieved what might be regarded as an almost impossible task, for their synopsis is surprisingly comprehensive and they have evidently been at great pains to state the essential facts briefly, with but few omissions and without using any undesirable contracted form of composition. It would obviously be unfair to compare such a book with a full-sized textbook running into three or four times as many pages, and it would be improper to criticize any lack of detail, for the aim of the authors has clearly been to enable the student to revise the salient facts of surgery rapidly before he faces the examiners.

The information provided is accurate and up to date; in matters where there is room for controversy the consensus of opinion has been well assessed. There are over 50 line drawings and diagrams of considerable value. A small criticism may be offered of No. 49, where more typical pyelographic diagrams might have been chosen, and of No. 56, where a tuberculous epididymitis is shown extending through the tunica and causing an anterior fistula in the scrotum instead of the characteristic postero-inferior sinus. The diagram of the fractured calcaneum also requires clarification. Is "Cromaffin" on p. 469 a printer's error or an Americanism?

On the whole this volume fulfils its purpose; it can be recommended to the student approaching his surgical finals for a last hectic review of the whole subject.

NORMAN C. LAKE.

CONGENITAL DISLOCATION OF HIP

Congenital Dysplasia of the Hip Joint and Sequelae. By Vernon L. Hart, M.D., F.A.C.S. (Pp. 187; illustrated. 36s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1952.

This book certainly has a message for the paediatrician, the obstetrician, and perhaps the midwife, for it is to them that the author looks for the early diagnosis of what we must go on calling by its old name until surgeons are able to prevent dislocation by treating the babies before it has occurred. The author's main object is to persuade his colleagues to look for the signs of "primary hip joint dysplasia" at birth in the pre-dislocation and, often, in the pre-subluxation stage, and he gives two main ways of doing this. First, the infant should be placed on its back in a state of relaxation induced by a bottle of milk while abduction of the flexed thighs is tested passively on both sides. Abduction to 80 degrees is normally possible, but dysplasia produces an adductor spasm which restricts this movement to a greater or less extent on one or both sides, according to whether the condition is unilateral or bilateral. Secondly, he depends on the "sign of the jerk" described by the Italian paediatrician Ortolani. He records this in detail, but, briefly, it consists in painless reduction and re-dislocation of the infant femoral head.

Either or both these signs call for an *x*-ray examination which will need careful and skilful interpretation, but which should enable the surgeon to form an opinion on the presence or absence of dysplasia. Infants with this condition are treated for a few months with the Frejka abduction pillow splint, which overcomes the adduction contracture in two or three weeks. Thereafter it maintains abduction in flexion for some months until there is *x*-ray evidence of improved ossification of the acetabular roof and the hip has become stable. This method is said to avoid admission to hospital, anaesthesia, manipulation, plaster-of-Paris or abduction frames, and to prevent subluxation,

dislocation, and all the other ills with which orthopaedic surgeons are only too familiar, even including abnormal anteversion of the femoral neck.

The rest of the book contains a general summary of the many views held from time to time on the aetiology and treatment of frank congenital dislocation of the hip and occasional quotations from past and present masters such as Putti, of Bologna, and our own Sir Thomas Fairbank. Some of this seems hardly germane to the author's purpose of following in Putti's footsteps by leading a crusade for earlier diagnosis. He does, however, go further than any of his mentors, not only by integrating their work, but by showing how diagnosis can be made quite simply at an early age by almost any doctor, and by recommending Frejka's pillow splint.

Orthopaedic surgeons need no conversion to the view that the earlier you treat the patients the better your congenital-hip results become, but they ought to read this well-documented and well-illustrated plea for increased co-operation from their colleagues in charge of the newborn. The author clearly believes that early diagnosis and treatment are now within reach, and that together they constitute the preventive surgery of congenital dislocation of the hip.

ERIC I. LLOYD.

HOUSING AND FAMILY LIFE

Housing and Family Life. By Professor J. M. Mackintosh, M.D., F.R.C.P. (Pp. 230; illustrated. 16s.) London: Cassell and Company. 1952.

The distinguished writer of this book has prodded us benevolently for a long time in his many excellent publications on preventive medicine. Here is further stimulation on the same high standard. I started reading the book as a task and finished it as a pleasure, and found it so full of new ideas and fresh views on old ones that I am firmly resolved to read it again, and perhaps yet again, in order to get the full flavour.

Professor Mackintosh gently reminds us of many things we ought to do and ought not to do. For example, he deplores the separation of the water-closet from the bathroom in the normal family house and gives cogent reasons for doing so. Two photographs show only too clearly the shadowing of windows of new buildings by overhanging eaves in one case and by balconies in another. It would have been interesting to have had the author's views about this, views which would be uninfluenced, of course, by the fact that in each case there was an award of a Ministry of Health Housing Medal, which was no doubt well merited for other reasons. The excellent paper does full justice to the printing of the illustrations. The plates include photographs of a variety of houses old and new. In two of them the Manchester streets, even though the photographs were taken on a dry day, are recognizable without the caption. But if the setts had only been glistening with rain, how much more convincing the pictures would have been to the non-Mancunian. This book is good and I would recommend that it be acquired, read, lent with discretion, and finally kept.

C. METCALFE BROWN.

FROM FIELD TO TABLE

Townsman's Food. By Magnus Pyke, B.Sc., Ph.D., F.R.I.C. (Pp. 212. 15s.) London: Turnstile Press Ltd. 1952.

The inhabitants of large towns depend for their food supplies on the successful carrying out of many complicated arrangements. Food collected in distant parts of the country, and even in remote corners of the world, must be wholesome and attractive after it has been transported, stored, and distributed. The time available between the collection of the food at its original source and its appearance on the urban table will depend on its perishability, and with foods such as milk and fish the processes which postpone deterioration for comparatively short times may be of great economic importance. Other foods, such as flour, cheese, and unripe fruits, may improve with time, and artificial processes may be devised to simulate the effects of storage. To preserve his products the food manufacturer may resort to the well-known methods of canning, drying, and refrigeration. To "improve" their quality he may also make use of a variety of chemical agents, some of which may prove to be less harmless than he had suspected.

In discussing such topics—and others relating to bread, meat, fish, chicken, eggs, ice-cream, fats, margarine, sugar sweeteners, fruit, and jam—Dr. Magnus Pyke is aided by both a wide range of experience and by a natural gift for writing. As a Principal Scientific Officer at the Ministry of Food during the second world war he watched the interplay of scientific knowledge, economic necessity, and popular prejudice in shaping official policy. In making decisions, he soon realized, the choice was usually not between black and white, but between shades of grey. If the wheat embryo was used to improve the quality of the national flour there must be a corresponding cut in the rations for pigs and poultry. Cheeses of the Stilton type might be highly nutritious and appeal both by taste and by tradition, but their production could not be allowed to impede the advance of social progress in providing milk for schoolchildren. While a sly sense of humour is occasionally given play, the author never seeks to contrast common human folly with his own wisdom, and concentrates on the modest presentation of facts rather than on attempts at propaganda. This book should make stimulating reading for the ordinary citizen, for whom it is intended, but few dietitians or others interested in nutrition will fail to find something that is both new and important to them.

T. MOORE.

HIGH BLOOD PRESSURE

Die Krankhafte Blutdrucksteigerung. By Professor L. Hantschmann. (Pp. 228; 33 figures. M. 36.) Stuttgart: Georg Thieme. 1952.

The title of this book is most nearly translated by "morbid high blood pressure." The author points out that the subject of this review is really a deranged vital function which leads to extensive independent pathological consequences. But at present it is difficult to grasp, for all the different pathological possibilities cannot yet be co-ordinated. Perhaps fewer monographs on this subject have appeared in German than in English, so on this ground the author considers some attempt is due. In the general part of the book he discusses in its first section the normal blood pressure and its regulation and variations. He then considers the causes of morbid high blood pressure, and he supports the idea that in increase of blood pressure, as suggested by Aschoff and some earlier writers, a true plethora plays a part. Pathological changes in vessels are the result and not the cause of hypertension. He discusses reflex causes in the central nervous system, and draws attention to the reflexes arising from urinary obstruction. The teaching and influence of Volhard permeate this book strongly. The author discusses the division of hypertensives into red and white types and gives some details of the differences in the capillary circulation of each. Perhaps we have paid too little attention to these generalizations; it may be there is something here that needs more study. There is some evidence that there are parallel differences in the kidneys themselves. The author's account of treatment is rather disappointing; little has been done as yet with the sympatheticolytic drugs—sympathectomy has not been very fully exploited. We in Britain hardly fear the provoking of Graves's disease by giving iodine. "Veratrum virile" is a curious misprint. There are a good many long case histories which are rather tedious and dully presented. But the book is worth reading, in part, if not all through, in order to gain some insight into the rather different points of view held on the Continent.

TERENCE EAST.

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AIR POLLUTION AND LUNG CANCER

Cancer of the lung has for many years been thought of as primarily a disease of town life, and, whenever it has been possible to break down national figures to show mortality rates separately for urban and for rural areas (as in England and Wales and in Denmark), the recorded mortality from lung cancer has consistently been higher in the urban areas. The excess may partly be accounted for by the greater facilities for diagnosis in the towns, but this would not appear to be the complete explanation, for, in England and Wales, the rates of increase of mortality have been closely similar in both types of area. To some extent the greater incidence in towns may be the result of the risks met with in the course of industrial employment, but no more than a very small proportion of the cases which occur in Britain can be attributed to the risks believed to be associated with the arsenic, asbestos, chromate, and nickel industries. A more substantial risk, from the point of view of numbers involved, is that encountered in the gas industry. From an analysis of national death certificates Kennaway and Kennaway[1] came to the conclusion that gasworkers suffer an unduly high mortality from lung cancer, and this has now been confirmed by Doll,[2] who studied the causes of death among a group of pensioners of a large London gas company. Doll found that gasworkers, as a whole, suffered a mortality from lung cancer approximately double that suffered by a comparable population of workers in all types of employment, but he was unable, from the limited evidence available, to determine whether there was any special employment within the gas industry where the risk was particularly concentrated. But the addition of the gas industry to the lengthening list of industries giving rise to specific occupational causes of lung cancer entirely fails to explain the high urban mortality from the disease. No common occupations, as, for example, motor-driving or building, have ever been incriminated as being responsible for above-average incidence, and there must be, so it would seem, some general factor common to all town dwellers. This, it is reasonable to suggest, may be found in the pollution of the atmosphere caused by domestic and industrial smoke.

Three types of carcinogen of proved potency are known to be present in atmospheric dust—namely, arsenic, benzpyrene, and the radioactive products of radium and thorium. The amounts present have recently been estimated in a series of investigations reported from Sir Ernest Kennaway's laboratories[3-5]; it appears that the benzpyrene derives largely from domestic chimney smoke but that the arsenic is dispersed to a considerable extent by industry. Gasworks are likely to be particularly suspect—both because of the increased risk run by their employees and because of the great excess of arsenic found in their neighbourhood.[3] However, McConnell, Gordon, and Jones[6] have shown, in a small group of 100 patients with lung cancer, that there was no greater tendency for such patients than for patients with other diseases to have resided near a gasworks.

Important new evidence of the existence of a carcinogen directly related to urbanization has now been produced by Stocks in an address to the annual conference of the National Smoke Abatement Society. He has found that standardized mortality rates from lung cancer for each county borough for the period 1946–9 are closely related to the number of inhabited dwellings in the area—particularly when towns which are actually contiguous are treated as a single unit. For example, the five groups of adjacent towns having more than 200,000 occupied dwellings (London, Manchester, Merseyside, Birmingham, and Leeds) gave standardized male mortality ratios of between 132 and 162 (as a percentage of the national rate), while three towns each with 40,000 to 50,000 dwellings gave an aggregate mortality ratio of 107, and 29 towns with less than 20,000 dwellings gave a figure of 89. The decrease in the mortality from lung cancer in men shows a quite remarkable regularity when compared with the decrease in the size of the towns, and much the same is also true for women, except that the decrease ceases below a town size of 40,000 dwellings.

It does not seem likely that so notable and steady a decrease could be due to differences in tobacco consumption, though there is a tendency for more tobacco to be smoked (and smoked in the form of cigarettes) in the larger towns. Stocks believes that the more probable explanation lies in the extent of the atmospheric pollution by domestic chimneys. He points out that the extent of such pollution

1 *Brit. J. Cancer*, 1947, **1**, 260.
2 *Brit. J. Industr. Med.*, 1952, **9**, 180.
3 Goulden, F., *et al.*, *Brit J. Cancer*, 1952, **6**, 1.
4 Waller, R. E., ibid., 1952, **6**, 8.
5 Dawson, K. B., ibid., 1952, **6**, 22.
6 *Lancet*, 1952, **2**, 651.
7 Stocks, P., *Brit. J. Cancer*, 1952, **6**, 99.
8 *British Medical Journal*, 1952, **2**, 710.

depends on at least three factors—the total number of dwellings, their concentration together, and the effects of wind. The association of the disease with the aggregate number of dwellings is clear, and the localization of the area of maximum incidence in the County of London in the neighbourhood of Stepney and Bethnal Green, north-east of the centre of the town, corresponds well with the W.S.W. origin of the prevailing wind. But the correlation postulated with density of population per acre is less convincing when calculated from the detailed figures.[7]

Though the case against chimney smoke is strong, it cannot be regarded as proved. Car exhaust fumes, for example, are also associated with urbanization, and there remains the obstinate fact that pollution from domestic smoke has become obviously less while the incidence of the disease has increased. It may be that the factor associated with urbanization is particularly effective when accompanied by an agent in tobacco smoke, so that the effect of the two combined is greater than would be expected from their simple addition. It is hoped that information on this point will be one of the fruits of the investigation[8] now begun by the British Empire Cancer Campaign in the Liverpool Hospital Region and in North Wales.

TUBERCULOSIS OF THE URINARY TRACT

The discovery of antibiotics and chemical substances which inhibit and destroy the tubercle bacillus raised high hopes that the treatment of tuberculosis of the urinary tract might be revolutionized. As is clear from the article by Mr. W. Galbraith which appears in our opening pages, early expectations have not been entirely fulfilled, but, in a complementary and ancillary role, these substances are a useful addition to surgery. Their value depends on the fact that urinary tuberculosis is always secondary to an infection elsewhere in the body. And only when the defensive mechanism of this primary lesion breaks down, allowing tubercle bacilli to escape into the blood stream and so reach the kidney, does the urinary tract become infected. Initially lesions in the kidneys are always bilateral. In most cases these foci tend to heal completely, but in about 5%[1] the lesion progresses to caseation and cavitation, or, by infecting the fornices of the papillae, ulceration extends peripherally into the parenchyma. The nature of the lesion will depend on the number and virulence of the organisms and on the resistance of the patient, but if the lesion progresses in one kidney the other kidney is likely to heal. Thus the introduction of substances which inhibit and destroy the organism in the primary focus as well as in the urinary tract are of especial value in raising the resistance of the body, which still remains the most important defence against this disease.

Unfortunately, except in the initial tubercle stage or early ulceration, the blood-borne drug can seldom reach the organisms in sufficient strength to destroy them. This is because the oedema and endarteritis of the chronic inflammation diminish the blood supply, and the drug certainly cannot reach those bacilli present in the caseous material. Thus the effectiveness of these substances is limited. Of the numerous antibiotics which have been prepared and tried out, streptomycin still remains the most widely used, owing to its efficacy and comparatively low toxicity in adequate therapeutic doses, in spite of the rapidity with which it produces drug resistance in the tubercle bacillus. The onset of this resistance in the bacillus was found to be considerably delayed by the administration at the same time of *para*-aminosalicylic acid, which has been used in the treatment of tuberculosis in Sweden since 1943. This drug had previously been used in combination with one of the thiosemicarbazone group of drugs with encouraging results, and in 1951 Cosbie Ross, Gow, and St. Hill[2] reported a series of cases in which thiosemicarbazone had been given at the same time as streptomycin and P.A.S. with success. More recently the introduction of isoniazid has given rise to much optimism and interest. Fortunately these antibiotics and chemical substances work well together and appear to be almost complementary to each other, so it is either in combination or in successive courses that they would appear to offer the most successful method of treatment.

In view of the difficulty in getting an adequate amount of the drug to the avascular tissue at the centre of an advanced focus, the indications for using antibiotic and chemotherapeutic remedies are limited, though some are clear: thus, when tubercle bacilli are present in the urine without any demonstrable kidney lesion the case usually responds well, the urine becoming free of bacilli and remaining so. If there is doubt about whether the pyelogram shows a definite tuberculous lesion, in so far as the outline of a terminal calyx is hazy or slightly clubbed, and the urine contains tubercle bacilli, then a prolonged course of medical treatment usually clears the urine of organisms and produces a more normal pyelogram. Even when there is a small ulcerative lesion of a calyx which is not amenable to partial nephrectomy,

[1] Band, D., *Edinb. med. J.*, 1942, **49**, 273.
[2] *Lancet*, 1951, **1**, 1033.
[8] *Postgrad. med. J.*, 1952, **28**, 78.
[4] *J. d'Urol.*, 1941, **49**, 385.

treatment by streptomycin and chemotherapy may arrest the progress of the lesion and render the urine free from bacilli. Finally, in cases of mild tuberculous cystitis with superficial ulceration, the symptoms of frequency and urgency are completely relieved by streptomycin and P.A.S. On the other hand, there are contraindications to the use of these drugs. Jacobs[3] believes that no benefit can be expected if they are given in cases of advanced bilateral renal lesions or advanced lesion of a solitary kidney, and that the risk of toxic symptoms and excessive cicatricial contraction should exclude their use. Contractions in the course of the ureter, especially at its lower end, may be increased by the administration of streptomycin. Again, in severe tuberculous cystitis with marked bladder contraction and ulceration this antibiotic is apt to increase the contraction. But isoniazid, with its low toxicity and absence of side-effects, is an antituberculous agent which has proved most useful in many cases in which streptomycin was contraindicated.

The most effective method of treatment still remains the total removal by surgery of the tuberculous focus. The most favourable type of case is that in which one kidney is infected while the other is healthy, but even then the survival rate is only 50% over five years, patients succumbing to the primary extra-urinary lesion or to a tuberculous infection of the remaining kidney. These facts make a strong case for pre-operative and post-operative antibiotic treatment, with six to twelve months in a sanatorium, the operation being performed at the peak of the patient's general condition, though Dos Santos and Bernard Fey[4] oppose early operation and wait until the function of the infected kidney has deteriorated and the healthier kidney has taken over its work. If the infection is bilateral, one kidney is often more disorganized than the other; it is then usually agreed that the more involved of the two kidneys should be removed. There is again some difference of opinion on whether streptomycin should be given in such cases before or after operation, although all agree on the need for prolonged sanatorium treatment. When one kidney is infected at one pole only, even if it is a solitary kidney, opinion increasingly favours carrying out a partial nephrectomy, with antituberculous medication before and after the operation. It is the case of gross bilateral renal involvement, with marked impairment of renal function as shown by intravenous pyelography, in which surgery is contraindicated, as also is chemotherapy. Involvement of the bladder by the tuberculous infection gives rise to a number of problems. The small contracted, ulcerated bladder causes extreme frequency of micturition which may amount almost to incontinence, while the pain and strangury reduce the patient to the limits of endurance. Chemotherapy and antibiotics are of little use, and suprapubic cystostomy is poorly tolerated by the intensely irritable bladder. Thus diversion of the urine either through the skin or into the bowel is the only method of affording the patient some measure of relief, though such procedures may be difficult when the ureter is grossly thickened, oedematous, and brittle, for these conditions increase the hazards of implantation considerably.

In spite of the excellent properties of the antituberculous agents now available, a drug is still required of high bactericidal and bacteriostatic power but of low toxicity, with great tissue penetration or with a predisposition to accumulate in tuberculous tissue. If a blood-borne chemotherapeutic agent had the power to increase the vascularity of the chronic inflammation surrounding the focus, it would obtain a closer contact with the tubercle bacillus and be considerably more effectual.

DEVELOPMENT OF CONSULTANT SERVICES

A detailed account[1] just published of the evolution, administration, and working of the hospital, ambulance, and first-aid services for England and Wales has particular interest because these comprehensive wartime services prepared the way for their counterparts in the National Health Service. The account merits careful study by those responsible for organizing the existing hospital and ambulance services to meet the present needs of peace and the possible future needs of war. Unnecessary mistakes have occurred too often in medicine because past records were unread. The highlights to the medical reader now are probably the chapters describing the emergency pathological service, the civilian blood transfusion service, radiology, and physical medicine. To most doctors under 40—and this includes many consultants—the rudimentary provision for these four specialties for the country as a whole before 1939 may be an eye-opener. We cannot be complacent about their progress since 1948, although the impetus of the progress of the war years was renewed under the National Health Service Act after the lost years 1946–8. In pathology and radiology there has been great expansion since 1948, and it is continuing; the blood transfusion service has been maintained and

1 *Medical History of the Second World War:* Emergency Medical Services: By Lieutenant-Colonel C. L. Dunn, C.I.E., I.M.S. (Ret.). Volume I, England and Wales. (Pp. 460; 16 plates. £2 10s.) London: H.M. Stationery Office. 1952.

improved; but the post-war history of physical medicine is more disappointing. Perhaps the medical profession has not yet absorbed Sir Robert Stanton Woods's teaching. He writes: "An unbiased observer must be impressed with the increased efficiency of physical medicine departments where the work is under the unified medical control of an expert. Before the war this condition hardly existed outside London. . . . The proper clinical function of the medical man in charge of a physical medicine department is twofold. Not only does his experience of the use of physical agents and of the more active forms of this therapy enable him to exercise expert day-to-day supervision of their application by technicians, but he is also in a position to form a necessary liaison between the rehabilitation department and the physicians and surgeons who have been responsible for the primary treatment of the patient and who continue to be responsible until the final results are attained." About 150 medical directors of physical medicine are required for England and Wales. Despite the lesson of the war, it is doubtful whether many regions have more than one-quarter of their proper quota, though great sums are spent in hospitals throughout the country on physiotherapy, largely undirected and much of comparatively little value.

The late Dr. A. E. Barclay's masterly account of radiology in the E.M.S. occupies only 10 pages. It is apparent how much of the great development of the post-war radiological service has followed from the wartime organization. Particularly notable is the expansion which has undoubtedly been possible only through the central generous supply of *x*-ray apparatus, apart from the normal capital allocation of the regional hospital boards. Dr. Barclay's scathing comments about the faulty planning of the standard *x*-ray departments for hutted hospitals—the plans not being seen by the consultant advisers until the buildings were well advanced—carry an important lesson for these days of regional planning. Full consultation is essential between local staff who are to run a department, and who can give, besides detailed local knowledge, much time to the individual problem, and the over-busy central office staff, who can give more expert knowledge of hospital planning in general and of the important financial aspects. Both must realize that the greatest wisdom does not lie with either alone but with both in combination, and usually in compromise. Dr. Barclay's final sentence bears thinking on: "Written reports from a radiologist are all right up to a point, but in a large proportion of cases personal consultation is essential if full value is to be obtained from the work done in the *x*-ray department." What would he have said about domiciliary consultations, so-called, where the general practitioner does not attend with the consultant?

An adequate staff of consultants resident within reasonable distance of the population served, and provided with the necessary local hospital accommodation and equipment, is an essential feature of the National Health Service. It received a tremendous fillip from the wartime dispersal of teaching; so did the idea of hospitals organized in large regions, each associated with one or more teaching hospitals. But the two ideas—adequate local hospital and consultant services, and association of peripheral hospitals with the teaching hospital in their region—do not necessarily go hand in hand so well now as they did in the wartime service. Indeed, one of the burning questions in the National Health Service at present is whether the teaching hospitals will have the breadth of vision to ensure that they do provide the valuable influence which they ought to exert in their associated regions. The peripheral hospitals are acquiring a full consultant staff much more numerous than the teaching hospital consultants and vying with them in quality, and these peripheral consultants may well become as sensitive about assumed superiority by teaching hospitals as were the senior doctors of the few great municipal hospital services in 1939. Regional associations of physicians and of surgeons, and so on, in which specialists from all types of hospital meet regularly and come to know each other personally, can do much to maintain friendly feelings and to spread the standards of the best consultants, whether they be teaching or non-teaching. Recruitment to the teaching hospital staff of outstanding consultants who have proved their worth in peripheral hospitals may be the only way for the teaching hospitals to maintain the intellectual and practical pre-eminence on which their regional influence must ultimately depend.

The most immediate problem arises from the present formal system of training consultants, foreshadowed by some wartime arrangements. Fair play is required now from the teaching hospitals in arranging their training schemes so that registrars and senior registrars spend part of their training period in teaching and part in non-teaching hospitals. It can be argued that this is necessary to ensure adequate training. And regional hospital boards, with their consultants, must not be driven to set up, as they could do, their independent training schemes for registrars and senior registrars. That would entail a great loss, and not least to the teaching hospitals themselves.

A DANGER OF BLOOD TRANSFUSION

It is one of the paradoxes of medicine that blood transfusion is both a cause and a cure of haemolytic disease of the newborn. Yet the paradox is an unnecessary one: if the same care that is given to the selection of blood for the babies were given to the choice of blood for potential mothers, transfusion would practically never lead to haemolytic disease.

Very soon after the discovery of the Rh blood groups it was realized that Rh-negative women could be immunized by transfusion with Rh-positive blood, and that this could cause their Rh-positive babies to suffer from haemolytic disease. For some years there was doubt about the magnitude of the danger. In 1946 Diamond showed that 46% of Rh-negative persons transfused with Rh-positive blood became immunized. Thus, if women of unknown Rh group are indiscriminately transfused with blood of unknown Rh group, nearly one-half of the Rh-negatives among them (who themselves, in England, amount to one in six of the total) will become immunized. Once immunized, a woman becomes and probably always remains unable to bear a healthy Rh-positive child. The serious responsibility borne by anyone who transfuses or injects blood into a female before or during child-bearing age has thus been fully known for some five years.

One of the first papers to stress the results of such transfusion as a public health problem was that of Discombe and Hughes.[1] They showed in 1948 that, whereas only 2% of unselected mothers had ever been transfused, 36% of mothers of babies with haemolytic disease gave a history of transfusion. It is easy to deduce that for this period, immediately after the war, and for a part of the London area, about one case in three of haemolytic disease was the result of transfusing an Rh-negative woman with Rh-positive blood. Most of the transfusions concerned were almost certainly given for air-raid injuries, and they were given at a time when the possible long-term dangers were known, if at all, only to a few research workers.

If in fact these dangers have become generally appreciated, a decrease is to be expected in the incidence of immunization by transfusion. In an investigation described in this issue Drs. W. Weiner and Vera Norris and Mr. S. Davidson have sought evidence of the occurrence of such a decrease. From the records of antenatal blood tests of the Midland Regional Blood Transfusion Service they have extracted the records of all Rh-negative women giving a history of having received a blood transfusion. The outstanding fact which they demonstrate is that, among Rh-negative women transfused in the years 1940–7, 41.7% were immunized, whereas of those transfused in 1948 and 1949 only 20.6% were immunized. Even if we subtract the 3.25% who (from the data of Weiner, Norris, and Davidson) would have been immunized by pregnancy alone, the first figure is near to that found by Diamond for transfusions in which Rh compatibility was completely disregarded. The second figure shows a very great improvement, but even after correction for natural immunization it implies that 17% of Rh-negative women receiving transfusions in the Midland Region in 1948 and 1949 were immunized by those transfusions. Since only about half of all Rh-incompatible transfusions are known to cause immunization, it is probable that over one-third of all transfusions of women in these years were still being carried out without taking account of Rh compatibility.

As the authors state, these figures are too high to be accepted with complacency. No woman should ever be immunized to the Rh factor by transfusion. The senior author, as Regional Transfusion Director, controls the supply both of Rh-negative blood and of anti-Rh serum for the region. The suggestions made for avoiding immunization can therefore be accepted as having full regard to the present supplies of blood and serum, not only for this region but for the whole country. They indicate that most transfusions can be planned, and Rh-negative blood reserved for Rh-negative recipients. In emergencies, every female who has not passed the menopause should be treated as Rh-negative until she has been shown to be Rh-positive, but a specimen of blood must be taken before transfusion is started, and immediate steps taken to carry out Rh grouping of the patient, and direct matching of all bottles of blood, including the first.

[1] *British Medical Journal*, 1948, **2**, 329.

ANTIBIOTICS IN THE TREATMENT OF LEPTOSPIROSIS

Hall and his colleagues[1] investigated the therapeutic action of five antibiotics—aureomycin, chloramphenicol, penicillin, streptomycin, and terramycin—in the treatment of human leptospirosis, and from their experience with 67 cases they concluded that these drugs had "no appreciable effect upon the clinical course of leptospirosis in man even when the drugs were administered relatively early in the course of the disease." Many other workers have expressed the opposite opinion, but when the published results are examined it is evident that most of the observers have treated only a small number of cases. Several reports have been made on the effect of penicillin. Baumann[2] treated 31 patients with this drug, and the number of cases in other reported series[3-7] varied from 16 to 4. In addition there are accounts of the treatment of single cases. It is also noteworthy that the stage of the disease at which the drug was first given varied widely. The need for early treatment is sometimes emphasized,[2 6] but in one case[8] penicillin was not given until the 30th day.

If the effect of treatment is to be measured by a reduction in the case fatality rate, only jaundiced patients should be considered, because spontaneous recovery is almost invariable in non-icteric forms of leptospirosis. When this criterion was used[9] the death rate in 152 jaundiced cases treated with penicillin was found to be 22%, compared with 23% in 103 cases treated before penicillin was available.

All these criticisms are applicable to the series described by Hall and his co-workers. Although the total number of patients treated was 67, the groups receiving the different antibiotics were of course smaller. Twenty-four were given aureomycin (13 aureomycin alone, 9 with streptomycin, and 2 with cortisone); 18

were given chloramphenicol; 12 streptomycin; 8 terramycin; and 5 penicillin. Thirty-nine of the 67 patients did not develop jaundice, and only the mean of the number of days which elapsed between onset of symptoms and beginning of antibiotic treatment is recorded for each group. A further 12 patients who received no specific therapy were included as controls for comparison, but none became jaundiced and all recovered. Finally the series included cases infected with *Leptospira icterohaemorrhagiae, L. bataviae, L. canicola,* and with an unidentified species. Two of the treated patients died. One was moribund when admitted to hospital on the seventh day of illness, and he died four hours after the first dose of aureomycin and cortisone. It would therefore seem reasonable to disregard this case. The second, a chronic alcoholic, died on the twelfth day of disease after seven days' treatment with chloramphenicol. When all these facts are taken into consideration it would not appear that the sweeping conclusions reached by the authors are justified.

Other evidence on the action of the newer antibiotics is scanty. There have been reports that aureomycin quickly controlled the infection in a few single cases,[10-12] but Broom[9] records one death among three patients so treated. In his series, four out of five patients recovered on streptomycin therapy, but two treated with chloramphenicol both died. In another short series[13] two of three patients died in spite of treatment with streptomycin. Terramycin[14] apparently produced rapid improvement in one patient whose condition was deteriorating steadily. Since no useful conclusions can be drawn from these meagre data, it seems worth considering the results of experiments in animals, even though they may not be directly applicable to man. Uhlenhuth and Schoenherr[15] treated golden hamsters infected with *L. canicola* with chloramphenicol, or aureomycin, or terramycin. Chloramphenicol was completely ineffective, but the other two drugs were curative even when administration was delayed until definite signs of infection were present. Terramycin was the more effective of the two, and is advocated by the authors as the drug of choice. Other observers[16] determined the minimal lethal concentrations of these antibiotics for leptospires *in vitro*, and compared them with the concentrations which can be obtained in the blood by therapeutic administration. Their findings indicated that the chloramphenicol content of blood was too low to be effective, but that aureomycin and terramycin could have a therapeutic action. To test this theoretical conclusion a single *in vivo* experiment was carried out on hamsters infected with *L. icterohaemorrhagiae*. It was found that the animals could be cured with terramycin even when treatment was withheld until the hamsters were manifestly sick.

From this brief survey it is clear that no dogmatic statement about the treatment of human leptospirosis with antibiotics is justifiable. Further experience alone can decide whether the results of aureomycin and terramycin therapy in man will parallel those observed in animals, though on the evidence available it appears that these drugs are the best at our disposal.

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NOBEL PRIZE, 1952

Dr. Selman A. Waksman, professor of soil microbiology at Rutgers University, New Jersey, has been awarded the 1952 Nobel Prize for Medicine for his discovery of streptomycin. His interest in the chemistry of living processes began many years ago in Russia—he was born in the Ukraine in 1888—and by 1915, five years after his arrival in the U.S.A., he had already undertaken a study and classification of the actinomycetes. His investigations were mainly agricultural until 1939, when René Dubos, who had been one of Waksman's students at Rutgers University, isolated from a spore-bearing soil bacterium a substance (gramicidin) which appeared to be capable of destroying pathogenic bacteria. About this time also Fleming's discovery of the antibacterial action of penicillin was being developed for therapeutic purposes, and Waksman turned his full attention to an attempt to isolate from the soil micro-organisms possessing antibiotic properties. It was early in 1944 that with Schatz and Bugie he announced the isolation from *Streptomyces griseus* of streptomycin, a substance antagonistic to both Gram-negative and Gram-positive bacteria, including *Mycobacterium tuberculosis*. The fact that streptomycin was the first effective antibiotic to be used in the treatment of tuberculosis has become a part of medical history. One of its most notable successes has been in tuberculous meningitis, no longer an invariably fatal disease.

A large proportion of the royalties which have accrued from the sale of streptomycin has been made over to the Rutgers Research and Endowment Foundation, where research in microbiology continues. Streptomycin has well-known limitations, among them its toxic effect on the eighth nerve and the development of resistance by tuberculosis bacilli. In reviewing the possibility of further advances in this field Dr. Waksman wrote in this *Journal*[1] two years ago: "Sooner or later other antibiotics will be found which are more effective than either [streptomycin and neomycin] and less toxic. The fact that in the various surveys on antibiotic production by micro-organisms the acid-fast bacteria are found to be among the most sensitive forms points to the possibility of the existence of such agents. Finding these is merely a matter of further search."

The next session of the General Medical Council will open on Tuesday, November 25, at 2 p.m., when the President, Professor David Campbell, will take the chair and will deliver an address.

1 *British Medical Journal*, 1950, **2**, 595.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

INTESTINAL WORMS

BY

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There are comparatively few inhabitants of this country who do not at some time in their lives harbour a worm, while indigenous peoples in the Tropics are seldom without one. Worms infecting man are of three classes: the Cestodes, or tapeworms; the Trematodes, or flukes; and the Nematodes, or roundworms. Of these, infections with cestodes and nematodes are the commonest; trematode infections other than schistosomiasis rarely occur. The present article is confined to cestode and nematode infections of the intestinal tract in man.

CESTODES, OR TAPEWORMS

The Beef Tapeworm

In Great Britain and in most parts of the world the commonest tapeworm found in man is *Taenia saginata*. This occurs wherever beef is eaten. Among peoples such as the Hindus, who do not eat beef, it is virtually unknown. The adult measures 3–4 metres in length, it attaches itself to the mucosa of the upper part of the small intestine by four suckers, and is divided into approximately 1,000 segments. The segments near the head are small and immature, the most distally placed, however, measure approximately 1.4 cm. in breadth by 2 cm. in length, and are equipped with male and female genital organs. Mature segments are motile when separated from the parent worm, and within each the uterus can be seen. The latter consists of a central stem from each side of which radiate between 18 and 30 branches. There is no communication between the uterus and the exterior, so that the eggs contained within it are liberated only by the disintegration of a segment. These eggs are infective only to cattle; they are not pathogenic to man.

Life History.—Cattle become infected when they graze on pasture soiled with human excreta containing eggs or tapeworm segments. The egg on reaching the animal's stomach develops into a larva which burrows into the mucosa, reaches a small blood vessel, and is then carried in the blood till it is held up in muscle or other organs. Here it develops into a cyst—the cysticercoid stage—and it is this cyst which is infective to man. On reaching the intestine of man the outer portion of a viable cyst is digested and the embryo within it develops into an adult worm.

Prevention.—Hygienic measures preventing the soiling of pastures by human excreta are most important. Thorough cooking will kill any cysticerci present in meat; many infected patients state that they have been in the habit of eating underdone beef.

The diagnosis of the infection is usually made by identifying segments passed in the faeces, and this is facilitated by placing one between two microscope slides, holding to the light, and examining with a hand lens. The lateral uterine branches appear milky white and may readily be counted. If there are more than a dozen the species is *T. saginata*, if less than this number it is *T. solium*. Eggs of *T. saginata* may be found in the faeces, but they cannot be distinguished morphologically from those of *T. solium*.

Symptoms of infection with *T. saginata* are usually few, and, in spite of popular belief, a ravenous appetite is very uncommon. Some patients may complain of dyspepsia and occasionally of nausea and vomiting. Most of those infected, however, seek medical advice because they have seen segments in the stool or because segments have passed through the anus by means of their own motility at times other than during defaecation. Occasionally the faculty of independent movement causes segments to become impacted in the appendix, with resulting local inflammatory disease.

T. saginata is the most difficult large tapeworm to expel, and unless the head is removed the parasite will grow again during the succeeding two to four months. As intestinal contents surrounding the worm may prevent the anthelmintic from reaching it, an important preliminary to treatment is to empty the alimentary canal as completely as possible. This also facilitates the identification of the head if it should be passed, there being little faecal material present to complicate the search. Accordingly for three days the patient should be given bland fluids without any solid food other than a finger of toast thrice daily. Magnesium sulphate, ½ oz. (14 g.), should be administered each morning during this period of starvation, and it is advisable for the patient to be in bed and preferably in hospital.

Extractum filicis liquidum is the most efficient anthelmintic in this infection, and the total dose for an adult is 90–120 minims (6–9 ml. approximately). This is divided into three equal parts and given at half-hourly intervals on the morning after completion of the starvation period. The extract is unpleasant to take and is therefore commonly supplied in gelatin capsules. As these may be carried past the head of the worm before their contents are liberated, it is advisable to prick the ends of the capsules before swallowing, or to give the drug in a draught. A prescription for the latter is ext. filicis liq., 90–120 minims (6–9 ml.); syr. zingib., 1½ dr. (5.2 ml.); and aq. menth. pip. to 1½ oz. (42 ml.). A still better method is to bring the anthelmintic directly in contact with the worm by duodenal intubation. After the usual starvation a Ryle's tube is swallowed and the patient is instructed to lie on the right side. In one-half to two hours the end of the tube is usually carried through the pylorus, though it is advisable to check its position radiologically. Two hours after the extract has been given a saline purge is administered (usually ½ oz. (14 g.) of sodium or magnesium sulphate). This serves the double purpose of expelling the worm and the anthelmintic once it has done its work. Little of the anthelmintic is therefore absorbed and toxic reactions are accordingly reduced in frequency.

In most cases the worm is passed between 2 and 12 hours after administration of the anthelmintic, and the head may be found at this time or during the succeeding two days. If, however, the head is not recovered it is unwise to repeat the course of treatment with filix mas until three months have elapsed, as the drug is toxic. A safe procedure is to give tetrachloroethylene after allowing the patient food for two days. This substance dissolves in fat and alcohol, in which it may therefore be absorbed from the intestine; the patient is accordingly placed on a low-fat diet and alcohol is withheld. Two days after the administration of the filix mas, 60 minims (4 ml.) of tetrachloroethylene is given in the morning on an empty stomach. Again administration as an emulsion or by a duodenal tube results in a higher percentage of cures than does administration in capsules. The usual saline purge is given two hours after the dose of anthelmintic. A prescription for the emulsion is tetrachloroethylene, 1 dr. (3.5 ml.); promulsin mucilage, 4 dr.

(14 ml.); spirit. menth. pip., 15 min. (1 ml.); aq. chloroform. to 2 oz. (57 ml.). Following treatment all stools are saved for 48 hours or until the head is found. Good results have recently been claimed for treatment with mepacrine; after the usual preliminary starvation, 100 mg. (1½ gr.) of mepacrine is given at intervals of five minutes until 1 g. (15 gr.) has been administered. A saline purge is given two hours later.

Other Tapeworms

Infections with *T. solium* are fortunately rare in this country. In treating them great care should be taken regarding disposal of faeces, as the ova, unlike those of *T. saginata*, are infective to man. In human tissues and brain they are able to develop into the cysticercoid stage of the parasite, and the cysts in the brain may cause epilepsy. *T. solium*, as well as the fish tapeworm *Dibothriocephalus latus*, may be expelled by the treatment already outlined. A curious, though uncommon, complication of infection with *D. latus* is severe megaloblastic anaemia. The worm apparently absorbs vitamin B_{12}, and if attached high up in the small intestine may divert this to itself before the human host has been able to absorb it. If situated some distance from the pylorus the host absorbs enough vitamin B_{12} to prevent anaemia before the intestinal contents reach the worm. Extracts of *D. latus* have been shown to have a high content of haemopoietic factor and to induce maximal reticulocyte crises in patients with pernicious anaemia.

NEMATODES, OR ROUNDWORMS

Of the family of Nematodes, or roundworms, the three commonest members infecting man are *Ascaris lumbricoides*, *Ancylostoma duodenale* (a hookworm), and *Enterobius vermicularis*, or the threadworm.

Ascariasis

Ascaris lumbricoides is not uncommon in Great Britain, though it is more prevalent in tropical countries. Infection is acquired by swallowing mature ova, which are usually conveyed on food and especially on uncooked vegetables. In the intestine the ova hatch out into larvae, and these, after burrowing into the intestinal mucosa, enter small blood vessels and are carried to the lungs, where they leave the blood stream and burrow through lung tissue till they reach a bronchus. They travel up the bronchus and trachea, over the epiglottis, and are then carried down the oesophagus to the intestine, where they mature into adult worms. The adult worms resemble earthworms in outward appearance, an adult male measuring approximately 25 cm. (10 in.) in length and an adult female 40 cm. (16 in.). A female ascaris passes approximately 200,000 eggs daily and 27 million during its lifetime. The infection is diagnosed by recognizing these eggs in the faeces. Occasionally an adult worm may be passed in the faeces or be vomited. Prophylaxis depends on preventing the contamination of soil by human excreta and, if this cannot be ensured, on the avoidance or thorough washing of vegetables eaten uncooked.

Bronchopneumonia may result from the passage of larvae through the lungs, but this is unusual unless a large number of ova are swallowed at one time. It is possible for a heavy infection to develop from swallowing small numbers of ova at intervals without the occurrence of lung symptoms. In light infections symptoms attributable to adult worms seldom occur, though occasionally there may be colic and the wandering habits of the worms may take them to the stomach, whence they may be vomited. Rarely they enter the appendix, common bile duct, or even the Eustachian tube. In some patients an allergic dermatitis occurs, presumably owing to the skin becoming sensitized to the worm's products. In heavy infections balls of worms may cause intestinal obstruction, particularly in children, and in those living on a poor diet worms may aggravate the state of malnutrition.

Treatment of Ascariasis

Several drugs are available, and the safest and most effective is hexylresorcinol. The adult dose is 1 g. (15 gr.), that for children of 2 to 4 years 0.4 g. (6 gr.) to 0.6 g. (10 gr.), and for those of 5 to 12 years 0.8 g. (12 gr.). Those older than 12 may be given the adult dose. The drug is taken in the morning, the patient having had nothing to eat since 6 p.m. on the previous day; it is advisable to follow the drug in two hours by a saline purgative. Hexylresorcinol is usually dispensed in capsules containing 0.2 g. (3 gr.), and these should not be bitten, otherwise the escaping contents will irritate the buccal mucosa. Tetrachloroethylene may be substituted for hexylresorcinol in an otherwise unchanged regime, but a disadvantage of this drug is that before killing the worms it stimulates them to great activity, and in children this might result in perforation of the bowel. In contrast to the treatment of tapeworms, there is not here the same necessity for an effective therapeutic action near the pylorus. Administration by duodenal tube or in an emulsion is therefore unnecessary, and the dose of 4 ml. (1 dr.) for an adult is most conveniently administered in gelatin capsules. Santonin has long been used in ascariasis, the adult dose being 0.2 g. (3 gr.) to 0.3 g. (5 gr.). This is administered nightly for three nights along with 0.12 g. (2 gr.) calomel, no special dieting being required. In some patients, even when small doses are administered, vision is disturbed, everything appearing either yellow or green. Fortunately this disturbance is rapidly rectified on discontinuing treatment.

Recently diethylcarbamazine ("hetrazan" or "banocide") has been used against this worm, and good results have been claimed. It may be given in tablets or in syrup. If the former are used the adult dose recommended is 18 mg. per kg. body weight daily for five days, the total daily dose being divided into three individual doses. Administered in the syrup, a single dose of 13 mg. per kg. body weight is given daily for four days.

Hookworms

Infections with the hookworm *Ancylostoma duodenale* are widespread throughout the Tropics and occasionally may be contracted in the temperate zone. In Great Britain this was the commonest worm infection found among troops and prisoners of war returning from the Far East. The male worm measures approximately 1 cm. by 500 μ, the female 1.2 cm. by 600 μ. The related species *Necator americanus* is slightly smaller and is widely distributed in the New World and in Africa. The worms may live for as long as six years, and it has been estimated that females produce up to 20,000 eggs a day. These eggs on reaching warm damp earth develop into larvae which are able to penetrate the unbroken skin. Infection is usually acquired by walking on such earth while wearing inadequate covering to the feet; very occasionally larvae may be swallowed. They bore through the tissue till they reach a blood vessel and are then carried in the blood to the lungs. There they burrow into alveoli and then migrate via the trachea and oesophagus to the duodenum, where they develop into mature worms, become attached to the intestinal mucosa, and feed on blood. The diagnosis is made by demonstrating the eggs in the patient's stool. Direct examination of fresh preparations will reveal all but very light infections, and for the latter concentration methods are available. In prevention, hygienic measures to limit contamination of soil by human faeces are of the utmost importance. The wearing of adequate covering to the feet and ankles will do much to prevent infection.

Symptoms are produced by the larvae penetrating the skin, by blood loss, and occasionally by the presence of worms in the intestine. The penetrating larvae irritate the skin and dermatitis usually occurs, often linear tracks may be seen, and the regions most affected are those between and adjacent to the toes and around the ankle. This dermatitis usually settles down without treatment in a few days.

Occasionally human skin may be invaded by larvae of *Ancylostoma braziliense*, a hookworm normally infecting dogs and cats. When this occurs a more chronic form of creeping eruption results. These larvae are unable to develop into adult worms in man.

The presence of adult hookworms in the duodenum seldom gives rise to symptoms, though occasionally mild dyspepsia may occur. The anaemia resulting from heavy infections is the main cause of debility and develops especially in those living on a poor diet deficient in protein. Its severity depends on the number of worms present and the adequacy or otherwise of the patient's diet. Among well-fed individuals even moderately heavy infections may be symptomless and the haemoglobin normal. Moderate degrees of anaemia are common among infected indigenous peoples in the Tropics, and severe anaemia is not infrequent among those who are malnourished. These anaemias are usually of the microcytic hypochromic variety, though it has been suggested that macrocytosis may result when the infected individual is obtaining enough iron in the diet. Helminthic infections in general and hookworm infections in particular may aggravate malnutrition in those on a poor or borderline diet.

Treatment should be directed to expelling adult worms and restoring to normal the blood picture and the state of nutrition. For the first, hexylresorcinol or tetrachloroethylene, used as for ascariasis, are equally effective. The latter readily responds to ferrous iron preparations and a well-balanced diet rich in protein.

Threadworms

Enterobius vermicularis is especially common in children and has a world-wide distribution. The female measures 1 cm. by 600 μ, compared with a mere 4 mm. by 150 μ in the male. The male dies after fertilizing the female, which migrates to the peri-anal region nightly and there deposits large numbers of eggs. These adhere to the skin in glutinous masses and are infective 36 hours after deposition. On being swallowed by man, the eggs develop into adult worms in the small intestine; an intermediate host is not required. Infective ova may survive in household dust and particularly in dust from the bedclothes of infected persons. Heavy infections are unlikely to arise from swallowing dust, but this mode of infection probably accounts for some of the extremely chronic infections met with from time to time.

The diagnosis may be made by finding worms in the faeces, and this is facilitated by giving a mild purgative. Ova may be demonstrated in material scraped from the peri-anal skin, a sharp spoon being used for the purpose. The National Institute of Health (N.I.H.) cellophane swab has been found of great value. It is fixed to a glass rod with a rubber band, and for use is moistened, rubbed over the peri-anal skin, and then transferred to the laboratory in a test-tube. The cellophane is spread out on a slide and examined directly for ova under the microscope.

During their wanderings on the peri-anal skin the female worms cause irritation which leads to scratching and which may disturb sleep. Through scratching, eggs may be conveyed to the mouth on fingers and behind the nails. As no intermediate host is required very heavy infections may be built up in this way. Appendicular inflammation occasionally results from migration of the worms.

Numerous remedies have been tried, but none are so effective as simple hygienic measures. The worms live for only three to six weeks, and if no ova are swallowed the infection will die out within this period. The most important single measure is to scrub the hands, including the nails, before every meal and after defaecation. The nails should be kept short. With the object of killing worms as they deposit ova on the peri-anal skin, this region should be smeared nightly with ung. hydrarg. ammon. Close-fitting pants worn at night will prevent any eggs laid from being scattered among other garments and bedclothes and mixing with household dust. These pants should be boiled immediately after use, and before beginning treatment bedclothes should be changed. Small nightly enemata of 2–4 oz. (57–114 ml.) of normal saline will rid the rectum and anal canal of worms likely to migrate during the night and will therefore prevent pruritus and contamination of fingers by ova.

Hexylresorcinol given in the dosage already stated is probably as effective as any anthelmintic, though unless treatment with it is combined with hygienic measures incomplete eradication of worms usually results.

Trichiniasis

Trichinella spiralis is commonly found in rats, occasionally in pigs, and man may be infected by eating undercooked infected pork. Outbreaks of trichiniasis in Wolverhampton and London in 1940 and 1941 were traced to the use of uncooked sausage meat as a sandwich spread. In the intestine the worm matures and bores into the mucosa, liberating larvae into small blood vessels. The larvae are disseminated throughout the body and encyst in a wide variety of organs. A peculiarity of this parasite is that its larvae encyst in the host harbouring the adult.

Symptoms are very variable, gastro-intestinal irritation and diarrhoea usually result from the presence of the worms in the intestine, and pyrexia, muscular pains, urticaria, and oedema from the disseminated larvae. Unfortunately only symptomatic treatment is of any value. Human infections can be prevented by thoroughly cooking pork, those in pigs by destroying rats, and by keeping pigs in rat-proof enclosures.

Other Roundworms

Strongyloides stercoralis and *Trichuris trichiuria* are intestinal worms less commonly affecting man than those already described. In all but heavy infections symptoms are slight or absent, and this is fortunate, as no known treatment is effective in eradicating them.

Discussion

Patients conscious of harbouring worms are usually impatient to have them expelled. It should be remembered, however, that their expulsion is not usually a matter of urgency and that all anthelmintics are toxic and treatment may be debilitating. It is usually wise, therefore, to postpone treatment of pregnant women till after parturition and of those ill from non-helminthic diseases till there is no longer a risk of their condition being aggravated by the treatment.

Treatment of helminthic infections in children may be difficult, as they often are unable to tolerate adult doses of drugs, yet the worms present may be fully grown. To children more than 12–14 years old, however, full doses of anthelmintics can usually be given, to those aged 5–12 years two-thirds to four-fifths of the adult dose, and to those aged 2–4 years one-half to two-thirds of the adult dose. Below the age of 2 years helminthic infections other than with threadworms are rare, and these may be adequately treated without the use of drugs.

Physicians are not uncommonly called upon to allay patients' unreasonable fears concerning helminthic infections. Worms appear to have a special psychological significance and an unusual ability to inflict psychological trauma. The latter is often out of all proportion to the physical disturbance produced. In some individuals this "alarm reaction" will be called into play by seeing in the faeces vegetable fibres superficially resembling worms; fortunately a brief microscopical examination will put the physician in a position to reassure such patients.

In children with convulsions the possibility of a worm infection being responsible is not uncommonly raised. Although convulsions have been ascribed to such infections, it is doubtful whether it is correct to do so except in cysticercosis, schistosomiasis, trichiniasis, and hydatid disease, in which larval forms of the worm may occur in

the brain. When convulsions occur in infections other than these, therefore, the possibility of their being due to idiopathic epilepsy should be carefully examined.

An eosinophilia usually accompanies the migration of larvae through the tissues. In the early stages of infection with worms in which such larval migrations occur an eosinophilia, often of marked degree, is present in the blood. A differential white blood cell count may therefore be of diagnostic value in infections with *Ascaris lumbricoides*, hookworms, *Trichinella spiralis*, and *Strongyloides stercoralis*. An eosinophilia also occurs in infections with *Trichuris trichiura*, schistosomes, and filariae, and if the contents of cysticerci are absorbed after death or after being damaged.

Next Refresher Course Article.—"The Diagnosis of Smallpox," by Dr. T. Anderson.

Refresher Course Book.—The first 55 articles of this series (fully revised) are available as a book, price 25s. including postage, from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Reports of Societies

HEART DISEASE AND PREGNANCY

Professor J. CRIGHTON BRAMWELL'S presidential address to the Manchester Medical Society on October 7 was on heart disease and pregnancy.

The risk of pregnancy in patients with heart disease depended, he said, on the severity of the disease. It could be assessed in most cases by the patient's tolerance for exercise prior to pregnancy. In patients whose heart disease was trivial the risk was negligible; in those whose tolerance for exercise was limited to a greater or lesser extent the added risk was appreciable; while in those who had suffered from heart failure the risk was considered prohibitive. Pregnancy was contraindicated in patients with active rheumatic carditis and in those whose cardiac condition was deteriorating rapidly. Intercurrent infections, especially bronchial infection and anaemia, were important and preventable causes of heart failure.

Chance of a Live Baby

The prospect of successful pregnancy must also be considered. In a recent series of 500 cases four out of five pregnancies had yielded living children, whereas in 53 patients who had advanced heart disease seen too late to terminate pregnancy, or who were unwilling for it to be terminated, only one in four was successful.

Acute pulmonary congestion in patients with mitral stenosis constituted a grave emergency which was liable to develop very suddenly and often proved fatal. If recognized in the first trimester, pregnancy should be terminated. Valvotomy was now a possible alternative to termination of pregnancy. In addition to the clinical evidence, *x*-ray screening was invaluable in the early recognition of this condition. Auricular fibrillation did not add so greatly to the risk as most earlier workers had imagined. Under favourable conditions it should not be regarded as a bar to pregnancy. In patients who had never actually had heart failure, but whose tolerance for exercise was considerably limited, assessment of the risk was most difficult, and factors other than the severity of the heart disease—namely, age and parity, temperament, and economic conditions—all had to be taken into consideration. The addition of an aortic lesion to mitral stenosis did not add to the risk. Opinions varied about the importance of cardiac enlargement, but many patients who died of acute pulmonary oedema had little cardiac enlargement. A case follow-up had shown that about 90% of patients who survived exhibited no evidence of cardiac deterioration as the result of pregnancy.

Treatment

Professor Bramwell believed that the two most important considerations in treatment were never to interfere with pregnancy in a patient with heart failure until everything possible had been done to relieve the heart failure, and, secondly, to ensure adequate antenatal supervision in every case. If heart failure was recognized early it responded well to treatment. In the antenatal clinic the almoner played a most important part. It was now known that blood volume and cardiac output diminished in the last few weeks of pregnancy, and that the strain on the heart was correspondingly reduced. There was therefore no cardiac justification for anticipating normal delivery by the induction of premature labour or caesarean section. All recent workers agreed that, in patients with heart failure, caesarean section carried a heavier mortality than normal delivery.

AETIOLOGY OF TROPICAL SPRUE

Sprue has always been difficult: it is an affliction of long-drawn-out misery, hard to treat and harder to understand. Its affinities with idiopathic steatorrhoea and coeliac disease are superficially obvious, and have often been emphasized. But we are still far from understanding the origins of all three. In his address to the Royal Society of Tropical Medicine and Hygiene on October 16, Professor A. C. FRAZER clarified some of the obscurities in a lucid account of investigations on all these conditions. There seems to be no doubt about the depressed absorptive capacity of the small intestine, which is not associated with any demonstrable organic lesion. There is, however, clear radiological evidence of increased secretion of mucus, and although this may be taken to indicate a catarrhal condition of the small intestine its precise significance is not yet clear. It is associated with decreased motility.

Professor Frazer could not answer the aetiological riddle of sprue, but suggested that the condition might be due to the use of rancid unsaturated fats. Rancidity might be present without affecting taste, and the geographical distribution of sprue coincided with areas where unsaturated fats are extensively used—it was rare where palm oil is a staple food. Rancid fats could cause steatorrhoea and increase secretion of mucus; the subject was now being investigated. He did not dismiss the idea of infection, which occurred to so many of the people who had observed the distribution of sprue in the Forces in India during the war, but there was no direct evidence of it. An association of coeliac disease with wheat gluten was clear and precise.

Professor A. W. WOODRUFF agreed that the vitamin-deficiency theories of the primary causation of sprue were untenable, and briefly stated the reasons why the disease known as sprue in the Caribbean might not be true sprue, but rather a megaloblastic anaemia of nutritional origin. Professor B. G. MAEGRAITH referred to his own experimental work on mepacrine, which in high dosage could give the same radiological picture of excessive secretion of mucus as Professor Frazer had described. He thought that the basic defect was in the absorption of fat, and had found absorption of glucose normal in some cases. Dr. F. D. ROSENTHAL emphasized the importance of failure of appetite in precipitating the onset of symptoms in the cases he saw in Hong Kong.

The Central Council for District Nursing in London is perturbed that the general public is not aware that 10% of the cost of running the home nursing service has to be provided by voluntary contributions. The demands on the service are continually increasing, and it would be unfortunate if its voluntary status were lost by lack of the necessary funds. It is felt that many of those who use the service would be pleased to make a donation if they were aware of the facts, and the Central Council would be most grateful for any assistance in this connexion. Donations should be sent either to the local associations or to the Central Council.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Intra-arterial Injections

SIR,—I read with interest your cautious annotation (October 18, p. 874) on the paper by Dr. H. S. Pemberton and his assistants (October 11, p. 808) on the intra-arterial injection of papaverine for arterial disease in the legs. As the head of the surgical side of the peripheral vascular clinic in which this work is done, I have watched with interest, and at first—I must admit—with not a little scepticism and alarm, the way in which my medical colleagues pumped this and that substance into femoral arteries. However, as I watched the results week by week, my doubts lessened and since I recently analysed the "before and after treatment" records I am completely convinced that they are obtaining results which are, at any rate, infinitely better than any other form of treatment, medical or surgical, has so far produced.

Clinical results gradually pointed to two drugs—tolazoline hydrochloride ("priscol") and papaverine—being better than any others, and further trial seemed to suggest that papaverine was the more effective of the two—an interesting finding in view of Kinmonth's results in arterial spasm. How often the injections should be given, or how long they should be continued, is still to be decided. In our clinic the results with intra-arterial histamine injections were not impressive.

While agreeing with you that spontaneous improvement may occur, it is equally true that the claudication may get worse. Of a series of patients with claudication, 34 were treated by intra-arterial injections of papaverine. Most of these patients said their claudication was getting worse, none gave any history of spontaneous improvement. After treatment with papaverine all but two were considerably improved, as proved by frequent testing of their walking distance on a moving platform "claudicometer" at two miles per hour. One patient showed no change over several months and another showed slight deterioration in the distance he could walk before pain began, but this may have been due in part to the fact that he had an intercurrent "stroke." Nine of the patients who, before treatment, got pain in the calf after distances varying from 54 to 274 metres (60 to 300 yards), walked over 800 metres (half a mile) without pain after papaverine injections. Twelve patients who had had to stop on account of pain after short distances were able, after treatment, to go beyond 800 metres.

The injection is simple, and, from my observation, causes less pain and fewer sequelae than intravenous injections in the arm. As a surgeon who has always been interested in peripheral vascular diseases, I am compelled to admit that intra-arterial injections of papaverine carry less risk and discomfort, and offer far more benefit in intermittent claudication, than sympathectomy has ever done. The results in cases of severe rest pain, or incipient or established necrosis, or gangrene do not appear to be any better than those obtained by conservative methods.—I am, etc.,

Liverpool. J. B. OLDHAM.

Lumbar Intervertebral Disk Protrusion

SIR,—I was greatly interested in Dr. D. M. Graham-Service's letter (October 18, p. 882). I sincerely hope that one day all medical students will attend demonstrations of the osteopathic type of manipulation as part of their training. The technique is easy to learn, is safe in correctly selected cases, and is spectacular in its relief of symptoms.

I do not agree with Dr. Graham-Service with regard to the number of manipulations required. Most backaches, whether caused by simple muscle strains, myalgia, fibrositis, sacro-iliac or lumbo-sacral strains or subluxations, will respond to one single manipulation. Too frequent manipulation can, in my opinion, cause a stretching and slackening of the ligaments supporting the sacro-iliac and numerous intervertebral joints. Admittedly, severe spasm will occasionally necessitate repeating the manipulation, but I find that preliminary infra-red radiation with gentle massage for a few minutes and occasionally a small local injection of procaine are a great help in overcoming spasm. The clicks that operator, patient, and onlookers hear are of no significance, but are of enormous psychological value.

The simple tears of the outer fibrocartilaginous portion usually respond well to manipulation. Where there is a herniation of the jelly-like nucleus pulposus I prefer to rest the patient, either in bed or in a plaster jacket. In the great majority the herniation appears to reduce itself, and only those who fail to respond to rest are sent to a neurosurgeon for an opinion as to the advisability of surgery.

I agree with Dr. Graham-Service that it is most important to train the patient to strengthen his own back. Physiotherapy, exercises, posture correction—including building up a heel if any pelvic tilt is present—and the avoidance of precipitating factors are all more important than artificial support, but in some patients with lax backs recurrences will occur in spite of all our efforts, and in these constant and efficient support is advisable.—I am, etc.,

London, S.W.16. HARRIS AVERY.

SIR,—I was sorry to read Dr. D. M. Graham-Service's letter (October 18, p. 882) praising osteopaths' views on the aetiology of sciatica. Once again the subluxated vertebra raises its discredited head, and displacement at the sacro-iliac joint is stated to cause root-pressure. Such a hypothesis transgresses anatomical fact. It is the disk—invisible on the skiagram—that lies in a position where it can exert root-pressure. The bones themselves cannot move out of alignment without this fact becoming immediately apparent on *x*-ray photography.

While it is true that osteopaths and other laymen can, and do, reduce a displaced fragment of disk, they labour under great difficulties. In the cervical region several of their manœuvres are directed to moving the atlas or axis. Luckily they do not have this effect, but they hurt the patient to no purpose. Since osteopaths do not use traction properly for cervical and thoracic reductions they fail needlessly, and occasionally increase the protrusion, thus causing severe pain. They have their successes at the lumbar spine, but again their lack of medical knowledge may cause failure, since they may choose the wrong manipulation, or carry it out at a faulty level, or waste time on irreducible protrusions. They benefit, on the other hand, by avoiding general anaesthesia, which, by preventing the continuous assessment of the result of each manœuvre, much increases any manipulator's difficulties.

Surely the time is over when our profession need by neglect let quick cures add to the triumphs of jubilant laymen? If a bonesetter's manipulation has cured a patient, then the same measure performed by a medical man, or a physiotherapist at his request, would also have led to recovery. The manipulations themselves are no secret; several illustrated books apart from my own are on the market. In disk-lesions, whenever possible, immediate reduction by a doctor or a physiotherapist represents my policy at St. Thomas's Hospital. There, for the last eight years—and before the war under Dr. Mennell—all our students of physiotherapy have been grounded in, amongst other manual techniques, spinal manipulation. The medical students witness these treatments and observe their results.

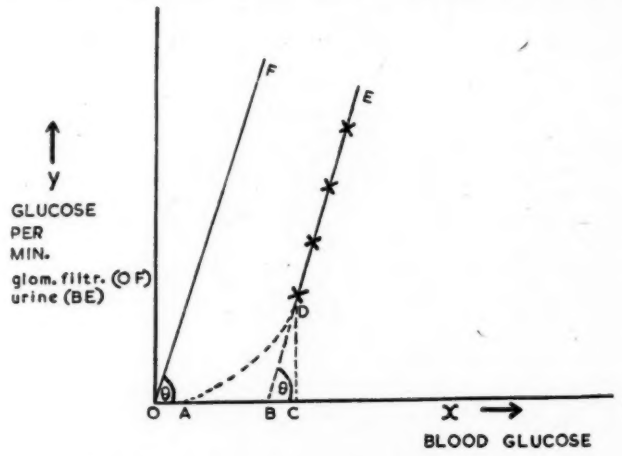
The bonesetters have had a long start, but, with the good will of the whole medical profession behind her, the ethical physiotherapist should be able to make up leeway quickly. Doctors should know that these methods were incorporated in the physiotherapy students' curriculum a few months ago. The time approaches, therefore, when doctors can order manipulation in suitable cases, and physiotherapists trained in these techniques will serve to make osteopaths and their like superfluous.—I am, etc.,

London, W.1. JAMES CYRIAX.

Tubular Reabsorption of Glucose

SIR,—Thank you for presenting Professor P. Govaerts's discourse (July 26, p. 175)—quite the best paper we have had on renal physiology for a long time. The graphs he has constructed are of the greatest interest and the manner in which values for the filtration, threshold, and maximum tubular reabsorption (TmG) are deduced are both fascinating and convincing. There are, however, certain difficulties in accepting his interpretations, especially as applied to the significance of the curve AD in my diagram. I feel his interpretation requires amplification if we are not to view it as unwarrantably hypothetical. The same applies to his use of the terms "maximum," "minimum," and "mean" threshold values.

Let us suppose that the four points along ED in my diagram have been actually plotted for a given subject. They demonstrate with adequate clarity the linear relationship observed between blood glucose (abscissa) and urinary glucose excreted per unit time (ordinate), *provided that the blood-sugar value is high*—i.e., greater than the value OC in the diagram. Thus, the straight line DB is purely imaginary and the distance OB, which Govaerts terms the "mean threshold," might be defined more accurately as the "extrapolated threshold." It is the value the threshold



would have if the linear relationship between blood glucose and urinary glucose excreted per unit time were maintained at low blood-sugar values. But the linear relationship is not, in fact, maintained. For low blood-glucose values, the observed relationship is represented by the curved line DA, not by the extrapolated line DB. It would therefore be legitimate to describe the distance OA (which Govaerts describes as the "minimum threshold") as the "observed threshold."

The straight line OF need not cause us anxiety in this argument. It represents the observed relationship between blood concentration and urinary excretion per unit time of a "non-threshold" substance such as thiosulphate. It also represents what the relationship between blood glucose and urinary excretion of glucose per minute would be if the entire tubular reabsorptive mechanism had been abolished—e.g., by poisoning with phlorhizin. In other words, OF represents glomerular filtration. To return to the curved line AD, in which lies the crux of the difficulty. Without invoking the differential calculus notation, Govaerts, in effect, postulates that the slope of the curve AD at any given point on it divided by the slope of EB (tan θ, "the filtration") gives us a value for the proportion of individual nephrons that are completely saturated at that particular blood-glucose value. At A the slope is zero, from which we are asked to conclude that no individual nephrons are saturated. At D the slope is a maximum, and we are asked to conclude that all the individual nephrons are saturated. In other words, as the blood sugar increases between OA and OC, the proportion of saturated nephrons increases from zero to unity and OB represents what the threshold would be if all the nephrons behaved uniformly. If this were the case, there would be no objection to defining OA as the "minimum," OB as the "mean," and OC as the "maximum" threshold values respectively. But what proof is there that this is the case? Is such a hypothesis anything more than highly speculative? Is one justified in applying a curve, based on information gained from the overall function of the renal mechanism, to interpret the behaviour of individual nephrons? To me this seems doubtful.

All I think we can say with certainty about AD is that the tubular apparatus—viewed exclusively as a machine for reabsorbing glucose—works less efficiently at low blood glucose values than at high ones. True, along OA all the filtered glucose is being reabsorbed, but that is a minor task, because so little is being filtered. Between A and B all the glucose filtered would also be reabsorbed if the machine were working as efficiently as it does at high blood-glucose levels; but it is not. Thus some glucose is excreted. When we reach the point D the machine now begins to work at its maximum efficiency, and from then on the linear relationship is established between urinary excretion of glucose per unit time and blood glucose. Beyond D (i.e., anywhere along DE) glucose reabsorption per unit time is constant and maximum (the TmG value of Govaerts)—that is to say, the machine will reabsorb the maximum amount of glucose it can and will excrete the remainder. From this argument it appears that the slope of AD at any point on it gives us some idea—how accurate I do not know—of the efficiency of the machine at a given blood-sugar value.

The problem therefore, as I see it, is why the tubular mechanism does not work really efficiently unless liberal quantities of glucose reach it through the glomeruli. It is possible that there may be a thermodynamical explanation for this, and it would be interesting to know whether one of your readers—Govaerts himself, perhaps—could provide one. In the meantime, I am sceptical about trying to predict the behaviour of individual nephrons from an essentially statistical graph, and must provisionally take the view that the renal tubules, like the teeth, work best when they have plenty to bite on.—I am, etc.,

Heathfield, Sussex. ADRIAN V. ADAMS.

"Pasteur's Flask" in Sydney University

SIR,—I was interested to see the article on the "Centenary of the University of Sydney" by Dr. Keith Inglis (August 23, p. 439), and to read of the flask containing a culture of bacteria brought to New South Wales in 1888 by my father, Dr. Adrien Loir.

Without any doubt the flask mentioned contained chicken cholera, and was prepared by my father, on Pasteur's instructions. Madame Pasteur had read him an announcement from the French paper *Le Temps* that the Government of New South Wales was asking for help to get rid of the plague of rabbits. The flask was not prepared by Pasteur, as Dr. Keith Inglis seems to think, but by my father, Dr. Adrien Loir, who was then attached to his uncle's laboratory. Pasteur had been paralysed since 1868 and did not do any manipulation himself in 1887, when the flask was prepared.

That this flask should now be considered a precious exhibit is all the more ironical when it is known that Dr. Adrien Loir was threatened by a fine of 10.000 francs and two years' imprisonment if he landed the culture in Australia without proper authorization. This news reached him by telegram, addressed to "Pasteur's nephew," when he touched Albany. Negotiations went on for months and made little headway. Meanwhile my father had to test the virulence of the microbes he had brought, as he was afraid that the long journey through the Red Sea, and the delay, might have attenuated them. As a laboratory he used the bathroom of a friend, Dr. Crivelli, who also procured two rabbits for test. Having no autoclave, my father kept the culture on himself, wrapped up in a flannel belt, for 48 hours—thus ensuring a constant temperature of 37° C.

After much delay and with the help of Senator Lamb, who took my father to Mr. Abigaël, the Minister for Agriculture, negotiations ended in the creation of a Pasteur Institute on Rodd Island, in the Bay of Sydney. This was the first Pasteur Institute founded on British territory.—I am, etc.,

Colchester. LILIAN A. BATES.

The Patient's Verdict

SIR,—Lord Moran is reported (October 25, p. 936) as saying in the Harveian Oration that the real remedy was not to pile up ways of impressing the patient, but to make it

unnecessary to win his favour. The physician of to-day, with his antibiotics, his sulpha drugs, insulin, liver extract, and the like, was fully armed and should have no need to impress the patient by more dubious means. . . . When the physician was independent of his patient the battle was won. . . . The system of merit awards to specialists meant that in future their promotion would depend less upon their patients' likes and dislikes and more on the verdict of their fellow consultants.

Sir, even in this modern world, I find these views surprising. The wisdom of the ages and the whole trend of research shows that any attempt to heal the patient's disease alone is doomed to failure; that only by making a man whole can he ever be well, and that the attempt to cure a man's physical ailments while leaving his soul sick can only increase confusion. And yet Lord Moran is in effect telling us that it does not matter to the patient whether the injection is given by a sympathetic friend or a bully. Surely the personality of the doctor and his understanding are the main factors in treatment?

In any case, what does Lord Moran mean by "fully armed"? Are we armed against cancer, tuberculosis, cold in the nose, rheumatism, hypertension, infantile paralysis, or a broken heart? If so, I am unaware of it. I am also unaware of any decrease in disease. Indeed, I am painfully aware of the opposite—for example, peptic ulcer and lung cancer.

It is no comfort to me to know that the awards committee has the matter in hand. I can only be thankful that Lister lived before he had to "obtain the verdict of his fellow consultants" as a condition of his advancement.—I am, etc.,

London, N.W.4. R. W. COCKSHUT.

Admission of Poliomyelitis Cases to Hospitals

SIR,—Your correspondents have gone to great lengths to justify the admission of cases of poliomyelitis to either general or fever hospitals. In this country it would seem that practically all such cases are admitted to hospitals, in addition about one-third as many more are admitted to hospital who are found not to have poliomyelitis. I would suggest that these are valid reasons for not sending to hospital every patient whose illness is suggestive of poliomyelitis.

There can be few more exhausting or frightening experiences for a child than being moved from its home environment to a hospital. It is generally accepted that these very conditions have an unfavourable effect on the progress of the disease. The fatigue and excessive handling of a journey to a hospital bed may perhaps change a non-paralytic to a paralytic case. Many such children could be nursed in their own beds by the child's own family under the direct supervision of the family practitioner, all of whom have the child's confidence. By the time the disease is suspected, the other members of the family will almost certainly be infected. The dangers from further exposure are probably negligible. Expert help in diagnosis, management, and aftercare can, in most areas, be obtained in the patient's own home or in out-patient clinics.

Generally speaking, the children who should be quietly nursed at home, provided conditions are suitable, are abortive cases (who often include siblings of known cases), and children with slight weakness only. Such cases form a significant proportion of hospital admissions. Immediate admission should be restricted to cases with more widespread paralysis or showing possible respiratory or bulbar involvement. These cases should be admitted to the hospital (general or fever) which, in the view of the practitioner, can provide the best nursing and medical care within the limits of distance. Your expert rightly states (September 13, p. 617): "The interests of the patient should take priority over the theoretical slight risks to others which are involved in sending the patient to a general rather than a fever hospital."—I am, etc.,

Huddersfield. W. P. SWEETNAM.

Inhalants in Bronchial Asthma

SIR,—We were interested to read the comments of Drs. Monica K. McAllen and H. Herxheimer (October 18, p. 879) on our article, and would like to reply to the points raised.

We agree that experiments have been performed as a result of which it has been claimed that isoprenaline is a more effective bronchodilator than adrenaline. We cannot agree that all our patients suffered from mild asthma. Some of them used the inhalants on an average 7 to 10 times during a 12-hour period. We cannot comment on the comparison of 2% to 3% isoprenaline solutions with neb. adrenal. et atrop. co., as the solution we used ("neo-epinine" No. 2) contains 1% w/v isoprenaline sulphate. If conditioned reflexes play a part in the relief obtained from inhalants, they presumably played a part for the good in the assessment of the isoprenaline solution when it was used 8, 9, or 10 times in a 12-hour period.

In conclusion, we can only repeat that in our experiment, in which the four inhalants were used as unknown solutions for a period of time and in such a manner that direct comparisons between them all were possible, no statistical or clinical difference in their effects was detected.—We are, etc.,

E. LEWIS-FANING.
Cardiff E. J. PARR.

Asthma in Childhood

SIR,—Dr. C. B. S. Fuller's article (September 20, p. 636) on asthma in children is valuable and instructive. He does not state his opinion about the tonsils alone, apart from the adenoids, as being the cause of asthma. It would be interesting to know this. It is my experience that the pathological adenoids are the important factor in keeping the nasal and sinus mucous membranes in an unhealthy state, and, by extension, the bronchial mucous membrane, as well causing a varying amount of respiratory obstruction and chest movement defects.

From custom the tonsils in children are commonly combined with the adenoids for criticism and execution, but this should not be so for several reasons. Further, I do not think that the adenoids (or tonsils if pathological) are a causative factor, but only a contributory factor. That has been my experience in my children with asthma. It is worth consideration that the greater operation of removing the tonsils might act as a trauma initiating asthma in a nervous child.—I am, etc.,

London, W.1. C. HAMBLEN-THOMAS.

Treatment by Radioactive Tantalum Wire

SIR,—It may be of interest to record one of the first cases of malignant disease other than of the bladder (which has already been reported[1]) to be treated by radioactive tantalum wire.

A man (a patient of Mr. F. D. Saner) aged 71, with a two months' history, was admitted with a large squamous carcinoma (biopsy) of the right cheek, including the adjacent parts of both lips, and infiltrating its whole extent. It was all grossly septic. He received *x*-ray therapy, 3,000 r in two weeks, which reduced the growth somewhat and improved the sepsis. A month later six lengths of radioactive tantalum wire were inserted at a spacing of 1¼ cm. to the whole area. The wire assumed the curvature of the lesion and, owing to its thin diameter, produced less tissue disturbance than radon seed chains, which have previously been used.[2] The reaction was similar to a radium implantation of the same tissue dose of 7,000 r in seven days. All induration and active growth seems to have cleared up at the time of writing.—I am, etc.,

London, N.7. ANTHONY GREEN.

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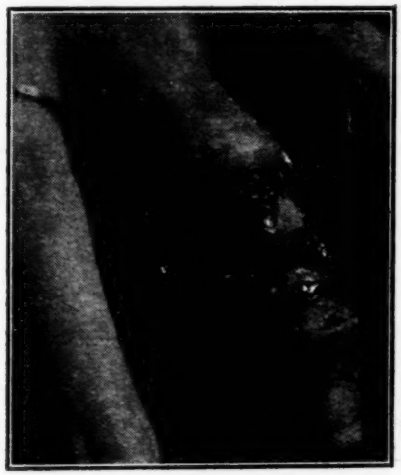
Treatment of Warts by Aromatic Vinegar

SIR,—Amongst the methods of treating warts available to the general public, the use of the preparation known as aromatic vinegar would appear to be attended by severe risks.

A female domestic servant, aged 22, reported on August 22 having (on the advice of a relative) applied aromatic vinegar to a wart (verruca vulgaris) 0.5 cm. in diameter on the dorsum of the middle phalanx of her right middle finger. She had applied the substance by inverting the bottle, and then touching the inner wet end of the cork on the wart. This manœuvre she had carried out once on the previous day and twice on the morning of August 22. She did not complain of pain, but the entire dorsum of the middle phalanx of the finger was pale and swollen. The tip of the finger was numb. The digit smelt strongly of acetic acid.



After thorough rinsing, saline soaks were applied and the finger was kept under daily observation. The following day there was oedema of the dorsum of the hand, but this settled down in two days. The skin over the affected middle phalanx soon broke down and sloughing began. On August 29 the proximal phalanx became a little inflamed. Systemic penicillin was administered and by September 2 all inflammation round the sloughing area had resolved. Sloughing continued, and on September 20 it was noted that the patient could no longer extend the terminal phalanx of the affected finger, destruction of the extensor expansion having occurred. A few days later periosteum and the distal interphalangeal joint were visible. *X*-ray examination on September 27 showed irregularity of the head of the middle phalanx. The patient was already under plastic surgical surveillance and was admitted for exploration of the finger under general anaesthesia. The likelihood of a useful finger resulting from treatment is very small, but attempts are being made to save it for cosmetic reasons.

Aromatic vinegar (*B.P.C.*) contains 74% v/v glacial acetic acid, with odorants. Like such escharotics as silver nitrate and trichloracetic acid it may be freely sold in a plain bottle. The importance of surrounding the wart, prior to treatment, with petroleum jelly is illustrated by this case, and it would seem desirable that when selling escharotics chemists should not fail to commend this precaution to their customers.—I am, etc.,

Retford, Notts. GORDON W. HICKISH.

Acquired Hypersensitivity to Sodium P.A.S., Streptomycin, and Penicillin

SIR,—The publication in your issue of September 20 (p. 647) of an article "Acquired Hypersensitivity to Sodium P.A.S., Streptomycin, and Penicillin," by Drs. B. Jeffery, P. Borrie, and N. Macdonald, prompts me to send you details of a similar case seen at this hospital.

The patient, a girl of 25, admitted because of a severe depressive psychosis, was found to have a tuberculous lesion at the left pulmonary apex. She had suffered from asthma since childhood. Sputum and laryngeal swabs were negative for tubercle bacilli. A course of electric convulsion therapy modified with a relaxant did not improve her mental condition. She was then put on streptomycin 2 g. twice weekly by injection, with sodium P.A.S. 18 g. daily in divided doses. On the second day of treatment she had a small rise of temperature to 99° F. (37.2° C.). Four days later she was given her second injection of streptomycin and the same evening her temperature rose to 103° F. (39.4° C.) and she developed a generalized erythematous rash. Streptomycin and P.A.S. were discontinued at once, the patient having received a total of 4 g. streptomycin and 90 g. P.A.S. On the following day leucocytes numbered 2,950, with 13% eosinophils, and the day after the temperature dropped to normal and the rash faded. On the tenth day after commencement of treatment her temperature rose again. She now had marked oedema and redness of the face, a confluent maculopapular rash most marked on the limbs, and erythema and fine desquamation of the back, later spreading round the trunk. The epitrochlear glands were enlarged. Nineteen days after commencement of treatment and 14 days after its cessation she became jaundiced and the lymphadenopathy generalized. By this time leucocytes had risen to 15,000, eosinophils 4%. The liver was palpable three finger-breadths below the costal margin. Van den Bergh reaction, direct positive; serum bilirubin 16 mg. per 100 ml. of serum. Paul-Bunnell test, negative. The urine contained a light cloud of albumin with bile salts and pigment; there were no casts or blood cells.

Subsequently the erythema gradually faded and was replaced by coarser scaling, the liver and lymphadenopathy regressed slowly together; leucocytes reached a peak of 19,250, eosinophils varying between 0%–19%. The temperature fell to normal by lysis in 10 days. Six weeks after first commencing treatment she was well, only some superficial scaling of the back remaining. A radiograph of the chest at the height of the illness showed no extension of the lesion, and a subsequent film two months later showed that it had resolved. Of further interest is the fact that at the height of her illness her depression cleared spontaneously, and was replaced by her usual attacks of asthma, which previously had been in abeyance.

The rapid onset of this patient's reaction after two peaks of temperature following streptomycin injections suggests that streptomycin may have been the aetiological factor rather than P.A.S. Our case differed from that reported by Dr. S. J. Steel (February 23, p. 415) in that toxic symptoms became apparent so early and in immediate relationship to injections of streptomycin, his patient receiving P.A.S. only; that the reaction proceeded as in his patient despite the immediate discontinuance of treatment in ours; and that neither pruritus nor lymphocytosis was marked. After a prodromal period lasting five days exfoliation commenced, followed after another five days by jaundice, hepatomegaly, and generalized lymphadenopathy. Unlike the case described by Dr. Jeffery *et al.*, renal involvement was not conspicuous in our patient, nor was there evidence of confusion or central nervous system involvement at any time. On the contrary, her pre-existing depressive psychosis cleared.

In another case, which Dr. Alan M. Edwards has kindly brought to my notice, an acute confusional state developed in a man aged 55 with advanced bilateral pulmonary tuberculosis after 10 days' treatment with sodium P.A.S. only. He also showed increased left-sided tonus with incoordination and an extensor plantar response similar to the case reported by Dr. Jeffery *et al.* Laboratory investigations, including cerebrospinal fluid examination, revealed no abnormality and the condition cleared within four days of omission of the P.A.S.—I am, etc.,

Napsbury, near St. Albans. RICHARD A. HUNTER.

Control of Bone Length

SIR,—In your annotation on control of bone growth (October 18, p. 872) you state that, "theoretically, epiphysial arrest is the ideal procedure in the growing patient" to equalize disparity in limb growth. Surely interference with the normal limb cannot be the ideal aim of treatment of a deformed limb? Theoretically the stimulation of bone growth within the defective short limb must be the ideal procedure.

Considering this to be so, we have for the last five years been engaged in this centre in a research on the stimulation of bone growth which can be effected by altering the blood flow within the bone. The encouraging results we obtained in animals have justified the first trials of this method in children, and we now seem to be on the way to being able to offer a method which is clinically practicable. The first accounts of this work were published in the *Bol. Soc. argent. Ortop. Traum.*, 1950, 5, 114, and in *La Readaptation des Enfants Atteints d'Infirmite Motrice*, recently published in

Paris. A paper read at the meeting of the International Society of Orthopaedics in Stockholm in May, 1951, is now to appear with the rest of the Proceedings of the International Society.—I am, etc.,

Nuffield Orthopaedic Centre, Oxford. J. TRUETA.

Operative Method of Thrombosing Varicose Veins

SIR,—I am grateful to Mr. Rowden Foote (October 25, p. 941) for bringing to my knowledge a reference in the foreign literature. As there seems to be no abstract available, I have had a translation made of the original article.

It appears that, unknown to Drs. S. T. Cortés and A. P. Rosas in South America (*Rev. Fac. Med. Bogota,* 1947, **15**, 629), I had been thinking along similar lines, and that, unknown to either of us, Mr. F. D. Murphy, of Bath (September 27, p. 725), had been doing the same. It is encouraging to note that both these authors report uniformly successful results.

Mr. Murphy states in his letter that he is having a larger elastic bougie made, with a globular end. In this connexion, it has occurred to me to use Buerger's dilating olives instead of the Babcock vein-stripper. They are a standard product, are relatively inexpensive, and I think should work well.—I am, etc.,

London, N.10. A. JOHNSTON ABRAHAM.

Ichthyosis and Hypnosis

SIR,—Drs. A. A. Mason and John Freeman seem to be at cross purposes. Surely Dr. Freeman (October 11, p. 832) is referring to ichthyosis simplex, for everything he says seems to indicate this. This comparatively common disorder is seldom severe and is often, as Dr. Freeman says, associated with the atopic eczema–asthma–hay-fever syndrome. It is familiar enough in skin clinics and can be influenced by a variety of treatments, both local and general, including quite possibly suggestion under hypnosis.

Dr. Mason's case (August 23, p. 422) of the rare erythroderma ichthyosiforme is different in every conceivable respect. I had the privilege of seeing the patient when Dr. Mason demonstrated him at the Royal Society of Medicine—and a very impressive demonstration it was—and I think the general reaction, like my own, was of more than surprise; it was fantastic, but true.

Erythroderma ichthyosiforme is a congenital disorder in which structural abnormality is more important than functional deviation; it is as much an anatomical maldevelopment as is clubfoot. It is surprising that it should respond to any kind of treatment; that it should respond to hypnotic suggestion demands a revision of current concepts of the relation between mind and body. If this case does not surprise Dr. Freeman, nothing ever will.—I am, etc.,

London, W.1. F. RAY BETTLEY.

Sickle-cell Anaemia in Africa

SIR,—Until we saw your annotation (August 23, p. 433) we were not aware that we were responsible for starting a controversy, and we should be glad if you all would allow us a few lines to clarify our position and reply to the letter of Drs. D. B. Jelliffe and John Humphreys (July 5, p. 42).

You quote as a further example of the rarity of sickle-cell anaemia (S.C.A.) in the negroes of Africa its absence in the Transvaal (Griffiths, 1952). But it is to be expected that S.C.A. would be rare or absent in this area, where the incidence of sickle-cell trait (S.C.T.) is less than 1% among the Mashangans who inhabit the Transvaal (Altman, 1945; and Murray—personal communication). The imported labour on the Rand is largely recruited from Portuguese East Africa south of parallel 22°, and from Bechuanaland and Basutoland. We have shown (Foy *et al.*, 1952) that in the natives from Portuguese East Africa, south of parallel 22°, the incidence of S.C.T. is never more than about 4%. We do not know the rates among the Bechuanas and the Basutos, but we believe them to be low. Presumably, therefore, the incidence of S.C.T. among the natives examined by Dr. Griffiths would not be more than 1%. The absence of S.C.A. in South Africa, then, bears out our view that high S.C.T. rates are probably of greater importance in determining the incidence of S.C.A. *in Africa* than in any admixture of white blood. We suppose that there is likely to be a greater admixture of Caucasian blood in South African negroes than, say, among the Luo of Kenya (S.C.T. rate 28%) or the Makuas and Makondas of Portuguese East Africa (S.C.T. rate 40%), and yet S.C.A. is absent in South Africa but present in the Luo and the Makuas and Makondas (Foy *et al.*, 1951a, 1952).

So far as we know, no evidence is forthcoming to substantiate the view that admixture of white blood is a determining influence in the incidence of S.C.A. *in Africa.* In fact, what evidence there is points in the other direction. We question whether you are justified in quoting the article of Hodges (1950) in support of Raper's suggestion, if only for the reason that no work done in Africa later than 1947 is mentioned by Hodges. Although it may be true that most of the negroes in the U.S.A. may have originally come from the West Coast of Africa, it should be realized that among these West African negroes the incidence of S.C.T. varies very greatly from place to place, which might have influenced Hodges's findings, even allowing for a considerable degree of intermarriage. His article also neglects the probable presence in Africa of intermixtures of Western negroes, Eastern negroes, Northern and Eastern Hamites, as well as Lacustrian and Eastern Bantus. Space forbids a complete analysis of Hodges's figures and conclusions, but we very much doubt whether they have any bearing on the situation in Africa, or the distribution of S.C.T. in this continent, or its relation to admixture with Caucasian blood.

We do not know what interpretation you put on the word "rare" in connexion with S.C.A.; whether you apply it to the findings of Lambotte-Legrand (1951) and Vandepitte (1952) in the Congo, to our findings in Kenya (Foy *et al.*, 1951a) or to the 22 cases seen by Drs. Jelliffe and Humphreys (1952) in 18 months on the West Coast. It is quite certain that S.C.A. occurs in the natives of Africa, but whether it does so in the expected proportion in all areas, as in the Belgian Congo and Kenya, remains to be seen. We have repeatedly stated that we do not consider the present genetical hypothesis takes into account all the known facts, particularly the occurrence of S.C.A. in individuals only one of whose parents has S.C.T., or only one S.C.A., even in cases where paternity can be reasonably regarded as certain (Foy *et al.*, 1951a, 1951b; Foy and Kondi, 1951).

Your annotation does not mention the desirability of being able to distinguish between S.C.T. and S.C.A., which is so important in mapping the distribution of the incidence of S.C.A. It is natural that S.C.A. should elude diagnosis in those countries where S.C.T. is common and may be grafted on to other profound anaemias that are not S.C.A. We think, however, that our findings of the development of long filamentous processes from the cells of cases with S.C.A. and not from those of S.C.T., as well as the presence of sickle cells in dry smears of peripheral blood in the former, should enable a differentiation to be made between S.C.A. and S.C.T. (Foy *et al.*, 1951a, 1951b; Foy and Kondi, 1951). Further, so far as we are aware, S.C.A. responds to no form of treatment, while other anaemias, grafted on to S.C.T., will respond to the appropriate treatment. We wonder whether the cases of anaemia that did not develop long filamentous processes, which Drs. Jelliffe and Humphreys mention in their letter (July 5) were really S.C.A. or other anaemias grafted on to S.C.T. Vandepitte and Pieters (1952) have dealt fully with the development of these filamentous processes in their latest paper. Whether S.C.A. is an important cause of death in African infants must, as we have already said (Foy and Kondi, 1952) await the collection of reliable data and vital statistics from the rural and urban areas of Africa.

We stated previously (Foy *et al.*, 1951b; Foy and Kondi, 1952) that it was our view that the suggestions of Seligman regarding the origin and migration of the African negro were, in some ways, incompatible with their ethnology as indicated by the distribution of S.C.T., always supposing that the sickle-cell phenomenon has an ethnological significance. The view of the eastern origin of the African negro is not a new one, as your annotation appears to imply, but was put forward in a somewhat modified form during the last century by Quatrefages (1887), Man (1885), Flower (1880), and Hüsing.

It is an over-simplification to say that the sickle-cell phenomenon was introduced into Africa from the East and

diminishes as one passes westward and southward from the Kenya Coast. Our studies in Portuguese East Africa show that in the north of this territory the incidence of S.C.T. among the Makuas and Makondas is 40% ; that there are great blocks of Eastern Hamites, Wakambas, and various groups of Bantu in central Kenya who have no sickle cells in their blood, and that the phenomenon reappears 500 miles west among the Nilotic Jaluos and the Bantu-speaking tribes of Northern Kavirondo. We shall shortly publish the results of a survey of all the major tribes of Kenya, Tanganyika, Portuguese East Africa, and the Southern Sudan, and we hope in this work to make an attempt to discuss whether the distribution of sickling agrees with the present ethnological classification of the African negroes.—We are, etc.,

HENRY FOY.
A. KONDI.

Wellcome Trust Research Laboratories, Nairobi.

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Drug Addiction

SIR,—I have been caused considerable embarrassment with members of the profession and others in regard to reports which have appeared in some daily newspapers to the effect that at a meeting of the North-East Metropolitan Regional Hospital Board on Wednesday, October 22, I stated that there were hundreds of thousands of barbiturate addicts in Britain, and, secondly, that barbiturate drugs could be purchased without prescription from some chemists.

I made no such statements or similar statements either at the meeting referred to or at any other time. I should greatly appreciate the courtesy of your columns in making this disclaimer.—I am, etc.,

JAMES GRAHAM,
Senior Administrative Medical Officer.

N.E. Metropolitan Regional Hospital Board.

POINTS FROM LETTERS

Wrapping the Journal

Dr. J. C. WOOLF (Wolverhampton) writes: The absence of a wrapping zipper has prompted me to employ the simple expedient of inserting a moistened thumb or middle finger into one end of the rolled *Journal*. By rotating the finger so as to tighten the spiral of the *Journal* the wrapper may be slid off from the opposite end with ease.

Dr. D. SAUNDERS (Cardiff) writes: I discovered by accident that the wrapper is easier to open than when the zip was present. Tear down half an inch of the wrapper at one end, grip the *Journal* with thumb and forefinger of one hand and with the corresponding fingers of the other hand grip the edge of the wrapper. The *Journal* will then pull straight out.

"Caking" of Soda Lime

Dr. K. S. THOM (Newport, Mon.) writes: I have to report a rather unusual cause of respiratory obstruction occurring during anaesthesia. A Coxeter-Mushin absorber was being used and, although relaxation was adequate, respiration was of the jerky diaphragmatic type and to some extent was interfering with the surgeon's laparotomy. Adequate oxygenation was obtained by assisted respiration, but the patient's condition was not entirely satisfactory. Examination of the soda lime showed that it had set almost into a plaster cast, although there was no undue moisture. It had not been in the canister for more than two or three days. . . . The counsel of perfection would appear to be to test the resistance of a closed circuit on one's lungs before inflicting it on the patient, but this is not always practicable.

Obituary

H. J. BURT-WHITE, M.D., F.R.C.S.

Mr. Harold Burt-White, who died in tragic circumstances on October 20 at his home in Salisbury, was gynaecological surgeon to the National Temperance Hospital, London, and to the General Infirmary, Salisbury. Harold Burt White (he changed his name to Burt-White in 1924) had an exceptionally brilliant career as a student at St. Bartholomew's Hospital, winning scholarships and prizes year by year as he went through the medical school and hospital. After graduating M.B., B.S. in 1924 he took the final F.R.C.S. examination in 1925 and proceeded M.D. in 1927 with the award of a gold medal. At St. Bartholomew's Hospital he won the Lawrence Research Scholarship in 1926 and 1927, and after holding resident posts he was appointed chief assistant to the gynaecological and obstetrical departments and senior curator of the museum. His original work on the bacteriology of puerperal sepsis was published in this and other journals. In 1930 he won the Bishop Harman Prize of the B.M.A. and in the following year the Nichols Prize of the Royal Society of Medicine, and he was elected a founder member of the Royal College of Obstetricians and Gynaecologists. By this time he had been appointed to the staffs of the City of London Maternity Hospital, the Soho Hospital for Women, and the Whipps Cross Hospital. Then in 1932 he was called to appear before the General Medical Council as a result of allegations that he had had improper association with a woman patient. Burt-White denied the charge, but his name was removed from the *Register*. Many of his former patients and friends organized petitions on his behalf, and in November, 1937, his name was restored to the *Register*. During the war Burt-White served in the R.A.M.C., and from 1942 to 1944 he was gynaecological specialist to the Women's Services in N. Ireland. Shortly after his demobilization he was appointed to the staff of the Salisbury General Infirmary as a gynaecological surgeon, and when the National Health Service began he became a consultant to the Salisbury group of hospitals, a position from which he had recently resigned. He practised also in London, both privately and as a member of the staff of the National Temperance Hospital.

J. M. writes: Harold Burt-White had an average school career, but his interest was awakened when he joined the premedical course at St. Bartholomew's Hospital in September, 1918, and from that point he became an outstanding student. From the start his interests were centred on surgery, and he devoted all his energies to the goal which he had set for himself. He was a hard and painstaking worker, and he possessed an excellent pair of hands, with the additional advantage that he was ambidextrous. He distinguished himself particularly during the course in anatomy, and he had no difficulty in passing the Primary Fellowship examination. His career in the wards was brilliant. He rapidly developed into an outstanding clinician, and his manual dexterity led to his becoming a skilful surgeon. After qualification he held various resident posts at St. Bartholomew's Hospital, and it was during his term of office as intern midwifery assistant that he developed his interest in obstetrics and gynaecology, which was later to become the supreme objective of his life. He contributed to the literature of his chosen subject, and he carried out an immense amount of work, both in hospital and in private practice. Although sometimes abrupt with

his colleagues, and tending to be intolerant with those whose minds were not so agile as his own, he was invariably kind to his patients, and he endeared himself to them by his gentleness and skill. Burt-White had few interests outside his profession. In a way this was a great disadvantage to him during the dark days which followed 1932, and his reaction to his misfortunes was such as to command admiration. He did not let himself go, but he did everything that could be done to preserve his skill and knowledge of his profession. His return, shortly before the war, made it even more difficult for him to re-establish himself, but at all times he worked hard, without relaxation, and it was this concentration of effort which was undoubtedly responsible to some extent for his untimely end.

Dr. R. C. LAWRENCE writes: May I be permitted to add my tribute to the memory of Burt-White? I had the privilege of serving as his anaesthetist during the late war and have very happy memories of his skill, punctuality, and unfailing good humour. Pre-eminently a gynaecologist, his energy was of the highest order and his attention to detail was scrupulous. "John," as he was always known to his friends in the Service, was a sincere, hard-working, and equable colleague and a man who will be sadly missed.

O'DONEL BROWNE, Litt.D., M.B., M.A.O., F.R.C.P.I., F.R.C.O.G.

Dr. MOHAMED SAID writes from the General Hospital, Seremban, Malaya: As one of Professor O'Donel Browne's postgraduate students who was in residence at the Rotunda Hospital from the beginning of April to the end of September, 1948, may I add my humble tribute in memory of a great master and a fine teacher, who was also kind, generous, and humane, to the obituary notice in the *Journal* of August 23 (p. 447) and to the appreciation by "W. R." in the *Journal* of September 6 (p. 567)? We were like a happy family at the Rotunda Hospital during those days, and the postgraduate students from overseas, who numbered among them three Indians, two Malays, two Canadians, two Englishmen, one Chinese, one Australian, one South African, one American, and one Armenian, were made to feel thoroughly at home. There was no doubt that the benign and pervasive influence of the master was at work in creating this happy atmosphere, and our six months' residence at the famous hospital was thus made memorable by the *camaraderie* that prevailed among postgraduate and undergraduate students alike and by the friendly, almost intimate, relationship that obtained between the master and assistant masters on the one hand and the postgraduate students on the other. Essentially kind and humane as he undoubtedly was, Professor Browne could be quite stern and unbending when the occasion demanded a display of firmness. I remember how on one occasion, following an unusually boisterous farewell party organized by undergraduates, he had us all mustered in the main lecture hall and gravely and sternly addressed us on the impropriety of our conduct and the necessity for moderation and self-control. With characteristic generosity, he sought to mitigate the severity of the blow for overseas students by remarking that too many Irishmen had attended the party. We emerged from the hall singularly chastened in spirit, but with an enhanced respect for the master. Professor Browne knew every undergraduate and postgraduate student by name, and was always generous in his offer of facilities for the latter, of whom he made it a practice to inquire if it was his intention to proceed to a higher degree or diploma and to tell him that he was ever willing to help. As a teacher, although he could deliver the usual didactic type of lecture with consummate skill, he chose rather to employ the Socratic method of question and answer at the bedside. He sought thus to emphasize the practical rather than the academic aspects of the subject, and employed this method of teaching with marked success during his Monday and Wednesday morning obstetric ward rounds and at his Thursday morning gynaecological clinics. He was possessed of a strong sense of humour and a ready wit. A postgraduate caught woolgathering while assisting him at a hysterectomy was gently pulled up with a line of Milton, "They also serve who only stand and wait"; and many were the apt quotations from Sterne and Goldsmith with which his lectures and talks were interlarded. I join his many former students in mourning the loss of a beloved master and teacher.

W. WATKINS-PITCHFORD, M.D., LL.D., F.R.C.S., D.P.H.

The death of Dr. W. Watkins-Pitchford was recorded in the *Journal* of October 11 (p. 834). We are indebted to Dr. A. J. ORENSTEIN for the following appreciation:

To the few still alive who knew Wilfred Watkins-Pitchford in South Africa, I am sure the outstanding memory is that of a lovable man of charm, friendliness, and kindness, quietly doing very competently an important and lasting job. Most of the people of South Africa, and particularly the miners, have probably forgotten him, but they owe him a lasting debt of gratitude. It was Watkins-Pitchford who laid the foundations of what is now the great Institute for Medical Research, and it was Watkins-Pitchford who established the Miners' Phthisis Medical Bureau, the first of its kind in the world. The pattern he laid down for the Bureau is the one still followed to this day—36 years from the time he was its first chairman.

Dr. EDGAR WILLIAM MATTHEWS, who died suddenly at Hove on October 3 at the age of 72, was born in London on May 5, 1880, and was educated at Kingston Grammar School, King's College, and King's College Hospital, where he qualified in 1906 and then held the posts of junior house-physician, senior house-physician, and house-surgeon. In 1909 he took the degrees of M.B., B.S. of the University of London and in 1920 he obtained the London D.P.H. After leaving hospital he travelled for a year in North and South America, Europe, and Africa, and then went into practice in Kingston-on-Thames. During the war of 1914–18 he was a member of the 3rd Home Counties Field Ambulance, R.A.M.C., and served in England and in France. Later he became commanding officer of the medical division of a military hospital at Chatham, with the rank of major. In 1919 he was appointed school medical officer at Kingston-on-Thames and two years later he became medical officer of health for the borough, where he did much to develop the maternity and child welfare services. A member of the executive committee of the Kingston Division of the B.M.A., Dr. Matthews was vice-chairman of the Division from 1928–30. He held the post of medical officer of health until 1937, when he resigned owing to ill-health. Two years before this he had retired from the Territorial Army with the rank of lieutenant-colonel, and was awarded the Territorial Decoration. After leaving Kingston he went to live in Sussex, and in 1939 he was appointed a member of the Brighton medical board, on which he sat until the day before his death. During the last war he also served as a captain in the Royal Sussex Home Guard and from 1942 to 1946 he was a part-time temporary assistant medical officer of the East Sussex County Council. In his younger days Matthews was an exceptionally good lawn tennis and hockey player. In 1907 he raised the first King's College Hospital hockey team to play in the inter-hospitals cup competition; he had also played for the United Hospitals and Surrey. For the last three years he was president of the Seaford Hockey Club.

Into a span of 88 years Dr. W. E. ST. L. FINNY, who died at his home at Kingston Hill on October 10, crowded a wealth of activities and interests that will remain in the memories of all who knew him. Born at Gotham, Nottinghamshire, of Irish descent, on September 1, 1864, William Evelyn St. Lawrence Finny was educated at St. Columba's

College and at Trinity College, Dublin, graduating M.B., M.Ch. at the Royal University of Ireland in 1887. In the same year he took the L.M. at the Rotunda Hospital, and in 1911 he obtained the M.D. of Queen's University, Belfast. After holding appointments under the Kent and the Nottinghamshire County Councils and at the Roxburgh, Berwick, and Selkirk District Asylum, Melrose, he settled in general practice at Kingston-on-Thames, but it soon became evident that work in the service of the community was to be the mainspring of his life. Becoming a member of the local board of guardians in 1894, he was elected to the borough council in 1897. A year later he became mayor and signified his pleasure in this appointment by presenting to the borough the chain of office now worn by the mayoress. On five subsequent occasions, in 1901, 1908, 1920, 1921, and 1926, the borough council re-elected him its chief citizen. For some 13 years Dr. Finny served as a councillor, and in 1910 he was raised to the aldermanic bench, in which position he remained until advancing years caused him to retire in 1949. Dr. Finny loved the borough, and never neglected an opportunity to make its name and its history well known far beyond its confines. Older Kingstonians will recall the pageants which he organized, particularly that celebrating the 700th anniversary of the granting of King John's Charter in 1200. It was a source of pride to Dr. Finny that in 1927 he was instrumental in obtaining from the late King George V the reaffirmation of the right of the town to use the designation "Royal Borough." Elected a member of the Surrey County Council in 1920, Dr. Finny did much work on its records and ancient monuments committee. It was through his efforts that the inventory of the borough's records was published. In 1944, for his many services, the borough elected him to the roll of honorary freemen, and in 1948 he became High Steward. He was also a freeman of the City of London, a barrister-at-law, and a justice of the peace. Dr. Finny loved ceremonial and was a stickler for its correct observance on all occasions as a means of keeping alive the traditions of the past. He had a life-long interest in photography, and was the founder of the Kingston Photographic Society, now the Kingston Camera Club. As a churchman Dr. Finny maintained a lively concern for all matters affecting Kingston parish church. He expended much time and labour in making known its history and in restoring its monuments and fabric. His success in tracing the site of the Saxon chapel of St. Mary, which adjoined the parish church on the south side, and which is reputed to be the church of the Saxon Coronations, will remain as evidence of his archaeological interests. He was a vice-president of the British Archaeological Association. During the war of 1914–18 Dr. Finny was a medical examiner under the Lord Derby scheme for recruitment to the armed Forces, and president of a recruiting board and of a pensions medical board. He was also civil medical officer at Kingston Barracks and at the local Territorial drill hall, and civil surgeon to the Kingston military hospital. He retired from practice some 30 years ago. He published a note-book on first-aid, which ran to three editions, in addition to a book and other papers on Kingston-on-Thames. Like most men of character Dr. Finny had his own views on matters, which he never lacked the courage to voice, but of those who may have disagreed with him, none doubted his sincerity. In his long life he served well the people of the Royal and Ancient Borough of Kingston-on-Thames. He leaves a widow and two daughters.—A. W. F.

The death of Mr. RALPH LESTER SCOTT occurred rather suddenly on October 14 at his home at Plumstead, Capetown, after a chronic illness of about two years' duration which had enforced his retirement from practice. He was born on January 10, 1885, at Calcutta, where his father was Master of the Mint, but the family home was at Boroughbridge, in Yorkshire. From Dundee High School he went on to Edinburgh University, where he graduated M.B., Ch.B. in 1907. He was elected F.R.C.S.Ed. in 1913. After house appointments at Edinburgh Royal Infirmary and at Liverpool, under the late Sir Robert Jones, he decided to specialize in ear, nose, and throat work, and had reached what would now be called registrar status in London when war broke out in 1914. He entered the R.A.M.C. at once and served throughout the war, being directed to general surgery for the duration of hostilities and becoming surgical specialist at No. 1 General Hospital at Étretat and later at Le Havre. On demobilization he resumed his chosen specialty and settled in practice at Capetown, where he rapidly gained recognition as a leading consultant. He became ear, nose, and throat surgeon to the New Somerset Hospital and to the Groote Schuur Hospital and lecturer in the University of Capetown. On retirement he was elected honorary consulting surgeon to the Groote Schuur Hospital. Scott was extremely thorough and conscientious in all his work and was particularly adept in obtaining the confidence of child patients, naturally an advantage in his specialty. He took great trouble to keep fully abreast of the progress of modern research, and visited England regularly to see for himself every new development of technique. His modest disposition and friendly approach made him popular with his colleagues, and his patients trusted him implicitly. He married Miss Ursula Schreiner, daughter of Mr. W. P. Schreiner, C.M.G., who was Attorney-General under Rhodes and afterwards Prime Minister of Cape Colony. Olive Schreiner, the novelist, was her aunt and Colonel F. W. Reitz her cousin. Mrs. Scott survives him with one daughter, who is training as a physiotherapist, and three sons, one a dermatologist in London and another in his final year as a medical student.

Dr. KARL FRANZ NAGELSCHMIDT, a pioneer in physical medicine, died in Manchester on October 4 at the age of 77. He had suffered a thrombotic attack in 1942 and again in 1945 and underwent an operation for cataract in 1948: from all these misfortunes he recovered and continued his work successfully up to within two or three days of his death. He was born in Berlin in 1875, and pursued his medical studies there and at Würzburg and Kiel, graduating in 1900. After the usual intern appointments he went to Copenhagen to study Finsen light, returning later to Berlin under Professor Lesser. After two years he moved to Breslau, where he worked with Professor Neisser. By this time he had made physiotherapy and electrotherapy his specialty, and he remained a specialist in this field for the rest of his life. In 1906 he returned to Berlin, being put in charge of the Finsen Clinic, where all physiotherapeutic methods were studied and used. At this time Nagelschmidt travelled extensively in Europe and America in order to study what was being done outside his own country. By 1933 he found himself unable to continue his work in the way he wished in Berlin, and for this reason he came to England, having paid several previous visits here. He took the Scottish triple qualification in 1937, and became a naturalized British subject in 1938. For many years he had been in charge of the physiotherapy department of the Manchester Jewish Hospital, and when that department was wrecked by enemy action in 1940 he reinstated much of his apparatus with his own hands. This work he continued until his retirement from the hospital staff in 1943. Throughout his life in Manchester he also conducted a well-known private clinic. Nagelschmidt's name must always be associated primarily with diathermy, a term which he himself coined and which has been generally accepted and used, but he made known his thoughts and works in many other fields of physiotherapy in a remarkably varied series of contributions to medical literature. The honour of being made a corresponding member of the Radiological Society of N. America gave him great pleasure. Nagelschmidt was very widely informed, and every meeting with him was an interesting and entertaining encounter. He was a considerable philosopher, with all the advantages of his polyglot upbringing, but above all else he was an enthusiast, for he worked incessantly and was always full of ideas. It may

be that his enthusiasm sometimes ran away with his judgment, but in these days of semitones a meeting with him was a particular pleasure because it had the same effect as a brisk walk against a high wind. He is survived by a wife, two sons, and a daughter, and his passing will leave a regretted gap for many.—G. J. L.

F. N. L. P. writes: In the obituary notice of the late Dr. W. J. MALONEY (September 13, p. 619) reference was made to a number of his earlier writings. It is not generally known that he spent the last few years of his life writing a new chapter in the history of paediatrics. An introduction to his projected work was published in 1950 with the title "John and George Armstrong at Edinburgh" (*Edinb. med. J.*, 57, 600), and he left the book which was written subsequently almost ready for the printer. Dr. Maloney's patient and extraordinarily thorough researches into the life and work of the Armstrong brothers convinced him that George was one of the greatest figures in paediatric history. His *Essay on the Diseases Most Fatal to Infants* (1767) is discussed by the historians, but only Haeser, the nineteenth-century German historian of medicine, had noted that he was also the founder of the first children's hospital in the world. From contemporary documents Dr. Maloney reconstructed the brief history of that institution—it treated some 35,000 infant patients in 10 years—and traced the tragic story (hitherto unknown) of George Armstrong's last years. He died in abject poverty, ruined by the expenses of his hospital, while his contemporary, Michael Underwood, won fame with his plagiaries from Armstrong's writings. With his characteristic passion for justice Dr. Maloney sought to right this ancient wrong, and his pursuit of this cause in recent years helped him to face long and severe illness with uncomplaining courage. George Armstrong was born at the manse of Castleton, in Roxburghshire, and there, in the village church, Dr. Maloney had erected a bronze tablet commemorating his achievements. He founded a "George Armstrong of Castleton Society," of which the local minister, the Reverend Alan Craig, M.A., is the secretary, and in the vestry of the church he had established an "Armstrong Museum" consisting of first editions of all the writings of the brothers and other relevant documents. It was Dr. Maloney's hope that paediatricians would take an interest in this historic birthplace and make it an object of pilgrimage when their travels took them to the north.

Dr. WILLIAM DOUGLAS, who died on October 1 at the age of 52, was born in Edinburgh. From Watson's School he went on to Edinburgh University, where he graduated M.B., Ch.B. in 1921. After holding resident posts at Bellahouston Hospital, Glasgow, he went into general practice, but his career was interrupted by the outbreak of war in 1939. Being already commissioned in the Territorial Army he was called up immediately, and he served for some years as a general duty medical officer, stationed at Hatfield House and Scarborough. In 1943 he was selected for training as a pathologist, and was graded as such with the rank of captain. At the close of hostilities he found his practice had disappeared in the London blitz, so after a short period in Cornwall he settled down in Sanderstead, Surrey, where he combined general practice with part-time duties in the B.O.A.C. immunization centre at Airways terminal. During the last four months before he was compelled to enter hospital he was struggling against intense pain, and only by the exercise of tremendous will-power was he able to carry on with his work. The end came six weeks later. A courtly and kindly man, Dr. Douglas was a fine shot and a better-than-average tennis player and golfer, but had not been able to pursue these activities for some years. He was not a man who sought friendship with all and sundry, but his loss will be felt all the more keenly by a small circle of friends, whose sympathy will be extended to his widow and two children.—K. H.

Medical Notes in Parliament

Food in Hospital

On October 16 Dr. BARNET STROSS asked what was being done to improve the diet of hospital in-patients, and what were the reasons for the low standard in some hospitals, homes for aged people, and day nurseries.

Mr. MACLEOD said that during recent years the standard of diet in hospitals, homes for aged persons, and day nurseries had much improved as a result of visits by dietetic advisers of the Ministry. Hospital authorities had also been advised to appoint experienced catering officers and to send their cooks on training courses.

Dr. STROSS further asked whether Mr. Macleod had recently been advised by his own Department that in some hospitals and homes the standard was too low because of lack of money and rising cost of food. He asked Mr. Macleod to pay attention to the kitchen equipment of institutions and provide money so that the kitchens might be reorganized and the technique improved.

Mr. MACLEOD said the Ministry had at least 250 reports in the last 12 months from hospitals, excluding day nurseries and other places.

Mr. G. R. STRAUSS intervened to ask whether Mr. Macleod knew that in many major London hospitals the poor quality of food and the unpalatable way it was served to patients who were severely ill were even to-day matters of widespread complaint.

Mr. MACLEOD replied that he was against generalizations in this matter. If he were given examples of hospitals he would make inquiries.

B.C.G. Vaccine

Mr. P. F. REMNANT asked, on October 16, whether B.C.G. vaccine was manufactured in this country.

Mr. MACLEOD said it was not. Manufacture would be considered as soon as the level of requirements justified it.

Mr. REMNANT pointed out that manufacture here was illegal under the Therapeutic Substances Act. A considerable amount was imported by air.

Mr. MACLEOD said he knew of this. The amount imported from Copenhagen and Paris at present totalled only £1,600 a year. Until the use of B.C.G. became more widely approved he did not think there was point in changing the present position.

Food-poisoning

Mr. VAUGHAN-MORGAN, on October 16, asked what steps the Minister of Health was taking, in conjunction with the Minister of Food, to offset the continued increase in outbreaks of food-poisoning.

Mr. MACLEOD answered that a major factor in dealing with this problem was recognition by both industry and public of the need for care and cleanliness in all aspects of food handling. Much publicity work had already been done. He had under consideration a revision of the Public Health (Infectious Diseases) Regulations so as to give wider powers in relation to food-poisoning.

Mr. VAUGHAN-MORGAN pointed out that, according to the report of the Ministry of Health, 83 of the 539 outbreaks last year had been in hospitals and institutions. He asked whether the Minister would take, to stop this, whatever disciplinary action was necessary.

Mr. MACLEOD answered: Yes, Sir, certainly.

Vitamin Fortification

Dr. BARNET STROSS asked on October 20 whether the Standing Committee on Medical and Nutritional Problems had reported on the possibility of excessive consumption of vitamins due to food fortified by these substances; and what conclusions had been arrived at.

Mr. MACLEOD replied that this report had been received and had been referred to the departments concerned for their consideration. It appeared from the report that in present circumstances there was no danger of excessive consumption of vitamins due to food fortified with these substances.

Lung Cancer and Gas Workers

Mr. S. T. SWINGLER on October 21 asked the Parliamentary Secretary to the Ministry of Works whether his attention had been drawn to the results of research by the Medical Research Council into the incidence of lung cancer among gas workers.

Mr. HUGH MOLSON replied that the Medical Research Council was aware of the results of an investigation into the incidence of lung cancer among gas workers, which was made through a statistical survey of the causes of death of the male pensioners of one of the largest of the former London gas companies. He had no reason to suppose that the conditions of work were different in other areas. The possibility of making further inquiry on different lines into this problem with a view to discovering any special causes of lung cancer in gas workers was being examined.

Agricultural Poisons

Sir THOMAS DUGDALE on October 21 moved the Second Reading of the Agriculture (Poisonous Substances) Bill. This Bill had already passed the House of Lords. He said it was designed to carry out recommendations made by the Gowers Committee on Health, Welfare, and Safety in non-industrial employment and by the Zuckerman Working Party on Toxic Chemicals in Agriculture. Professor Zuckerman had now gone on to study other aspects on which the Government needed advice, in particular the possibility of the effects upon people other than those directly concerned in the use of the chemicals to which the Bill referred. There were undoubtedly risks to the health of workers using certain poisonous substances as insecticides or weed-killers mainly by spreading, and Parliament had to see that these workers were given the greatest practical measure of protection. The Bill would allow Ministers of Agriculture to make regulations for that purpose.

A good deal had been done by advice, but the Government could not be sure that voluntary arrangements would be followed sufficiently widely. Last year the Ministry of Agriculture had agreed with organizations representing farmers and farm workers, agricultural contractors, and insecticide manufacturers on recommendations for voluntary observation of precautions. This year the same organizations had agreed on a revised scheme of precautions, and the Ministry of Agriculture arranged for five members of the outdoor staff of that Ministry's labour division to act as observers. These observers had given much information and advice to employers and obtained valuable information on current practice. If the House passed the Bill these men should be employed as inspectors under the Act.

A further aspect was the effect of these substances on wild life present when the spray was employed or feeding on the crops shortly afterwards. The Agricultural Research Council was concentrating on finding an insecticide which was not toxic to mammals or birds.

Up to the present the precautions had been generally effective. The Government proposed to make regulations at an early date after the passing of the Bill on the lines of these voluntary precautions.

Mr. A. J. CHAMPION said the trade unions catering for the agricultural industry desired the passage of the Bill.

Colonel GOMME-DUNCAN recalled that one or two men had died as a result of distributing these poisons on the land.

Dead Animals

Mr. ANTHONY HURD said the Bill did not go far enough. It took action to safeguard the health of men employed by contractors or farmers who used two types of spray—the dinitro compounds and the organo-phosphorous compounds. Both were deadly poisons if a man was in contact with them day after day. He regretted that the Bill did not prevent the use of these two groups of sprays until scientists could offer alternative and equally effective methods of dealing with weeds and insects. He gave an account of the death roll on one field of brussels sprouts of 46½ acres in which 175 dead mammals and birds had been picked up after the spraying of the crop. Until the scientists could offer alternatives, he would feel happier if the use of these two types of spray was prohibited. He was told they only amounted to about 10% of all the weed-spraying and insecticide-spraying which was done.

Mr. JOHN MORRISON hoped that men working with sprays would take particular care regarding protective clothing and of their arms. He was alarmed at the amount of spray which might go into their eyes. He suggested that if poisonous sprays killed all the weeds which have longer tap-roots farmers would lose the plants which brought up elements essential in animal food.

Sir THOMAS DUGDALE, replying to the debate, estimated that over 2½ million acres had been sprayed with weed-killers this year and that over nine-tenths of the acreage sprayed was treated with hormone weed-killers which were not very poisonous. Under the Bill there was power if necessary to prohibit the use of any weed-killer. The Agricultural Research Council was working hard to find an alternative to these very dangerous weed-killers.

The Bill was then read a second time without a division.

The Danckwerts Award

Mr. CROOKSHANK announced on October 23 that a debate was to take place on October 30 on the Danckwerts award.

On October 23 Mrs. JEAN MANN asked what portion of the Danckwerts award would be passed on to doctor assistants and trainee apprentices; and how far, in view of this award, Mr. Macleod considered it necessary to continue payments to doctors for trainee assistants.

Mr. IAIN MACLEOD could not say what adjustments in the light of the Danckwerts award would be made in the salaries of assistants, which was a matter for the doctors who employed them. He added that no changes were at present under consideration in the arrangements for paying grants to doctors who supervised the training of assistants. He would not agree that this was just a subsidy for locums. It had much more value than that. Both the original scheme and the Danckwerts award were attached to principals and not to assistants.

Major G. LLOYD said there was a difference of opinion in the medical profession on how these sums should be allotted. He asked Mr. Macleod to consider representations before the final recommendations were approved by the Government.

Mr. MACLEOD replied that he had already started to implement the award of the Danckwerts money. The vote had been passed by the House without comment before the Summer Recess, but he would be happy to consider any representations which were made on the matter.

Cortisone.—Controlled trials of cortisone in the treatment of rheumatic conditions are continuing, but a considered opinion as to its efficacy is not yet possible. Mr. Macleod hopes gradually to increase the quantities made available to the special hospital centres at which this drug is used.

Cost of Hospital Building.—The capital cost of new hospital construction and extensions in schemes approved in England and Wales since October last is £5,114,958. The corresponding figure for the previous year was £7,486,640.

Nursing Shortage.—The present shortage of nursing staff in the mental hospitals of England and Wales is estimated at about 3,500 men and 7,700 women. A year ago it was estimated at about 3,000 men and 8,000 women. The problem is being closely studied by the Mental Health Advisory Committee.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending October 11 (No. 41) and corresponding week 1951.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire	1951 Eng. & Wales	1951 Lond.	1951 Scot.	1951 N. Ire.	1951 Eire
Diphtheria	24	2	8	1		41	1	20	3	1
Dysentery	160	17	96	1	1	118	21	54	0	
Encephalitis, acute	3		0	0		5	0	0	0	
Enteric fever:										
Typhoid	2	1	0	0		6	0	0	0	0
Paratyphoid	25	0	0	0		90	3	0	0	
Food-poisoning	162	18		0		193	27		2	
Infective enteritis or diarrhoea under 2 years				18	25				9	60
Measles*	5,716	682	90	24	58	1,648	32	93	148	145
Meningococcal infection	40	4	14	0		35	3	18	1	2
Ophthalmia neonatorum	28	7	14	0		37	0	13	0	1
Pneumonia†	416	26	184	2	2	395	17	153	6	
Poliomyelitis, acute:										
Paralytic	92	8	12	7	10	54	4	9	5	2
Non-paralytic	17	3				40	4			
Puerperal fever§	256	56	19	1		251	42	15	4	
Scarlet fever	1,617	160	303	23	76	1,032	98	208	27	39
Tuberculosis:										
Respiratory			136	28				126	33	
Non-respiratory			21	5				29	4	
Whooping-cough	1,078	57	79	30	51	1,612	77	277	54	73

DEATHS in Great Towns	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire	1951 Eng. & Wales	1951 Lond.	1951 Scot.	1951 N. Ire.	1951 Eire
Diphtheria	0	0	1	0	0	*1*	0	*0*	0	0
Dysentery	1	1		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0		0		*0*	0	*0*	0	
Infective enteritis or diarrhoea under 2 years	6		3	3		*8*		*1*	0	0
Influenza	11	4		0	0	*9*	0	*0*	0	0
Measles		0		0	0		0	*0*	0	0
Meningococcal infection		0					1	*0*		
Pneumonia	169	27		3	3	*136*	18		12	4
Poliomyelitis, acute	7	0			0	*2*	0			0
Scarlet fever		0		0	0		0	*1*	0	0
Tuberculosis:										
Respiratory	81	8	11	2	6	*114*	24	*14*	1	6
Non-respiratory		2	3	1	3		2	*3*	0	2
Whooping-cough	2			0	0	*2*	0	*0*	0	0
Deaths 0–1 year	236	34	29	12	12	*187*	14	*23*	6	4
Deaths (excluding stillbirths)	4,771	697	524	97	171	*4,206*	649	*486*	89	124
LIVE BIRTHS	7,726	1225	952	234	44(	*6,479*	1051	*808*	204	358
STILLBIRTHS	196	19	27			*141*	19	*22*		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Infectious Diseases

The chief fluctuations in the trends of infectious diseases in England and Wales during the week ending October 11 were rises in the number of notifications of measles from 4,696 to 5,716, and scarlet fever from 1,284 to 1,617, and falls in whooping-cough from 1,126 to 1,078, and acute poliomyelitis from 155 to 109.

The incidence of measles has risen continuously during the past four weeks from 2,421 to 5,716 notifications. The largest rises during the week were Middlesex 165 (from 107 to 272), Lancashire 150 (from 630 to 780), and London 128 (from 554 to 682). The largest rises in scarlet fever were 49 in Essex (from 97 to 146) and 42 in London (from 118 to 160). No changes of any size were reported in the local trends of whooping-cough. The number of notifications of diphtheria decreased by 1 to a total of 24. The features of the local returns were a fall in Lancashire from 10 to 2 and a rise in Yorkshire West Riding from 0 to 6. In the latter county all the cases were notified in Thirsk R.D.

Cases of paratyphoid fever notified numbered 25, an increase of 2 on the total of the preceding week. In Wales the notifications rose from 11 to 18. The largest returns were Monmouthshire 12 (Tredegar U.D. 12) and Glamorganshire 5.

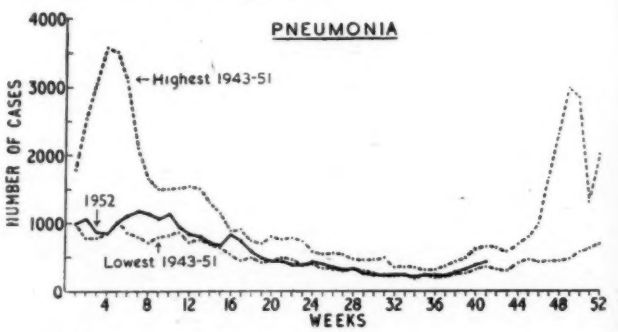
The notifications of acute poliomyelitis were 109, being 9 fewer for paralytic and 37 fewer for non-paralytic cases than in the preceding week. The largest returns during the week were Lancashire 11 (Manchester C.B. 4), London 11, Yorkshire West Riding 9, and Middlesex 9.

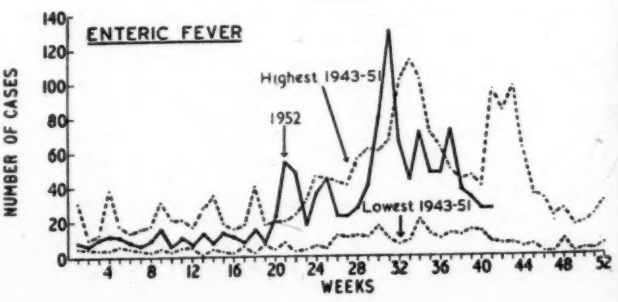
160 cases of dysentery were notified, 32 fewer than in the preceding week. The chief centres of infection were Lancashire 39 (Blackburn R.D. 11), Yorkshire West Riding 26, Lincolnshire 18 (Grimsby C.B. 16), and London 17.

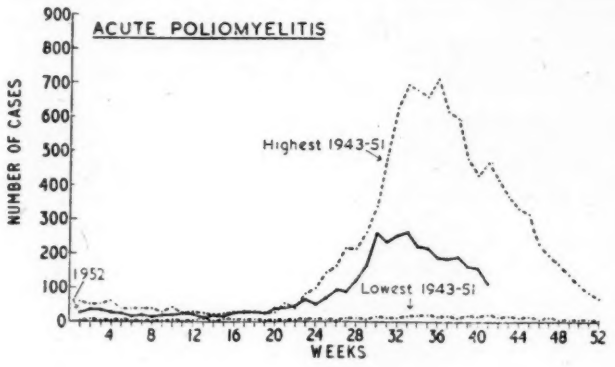
The largest outbreak of food-poisoning reported during the week was 41 cases in Yorkshire West Riding, Penistone R.D.

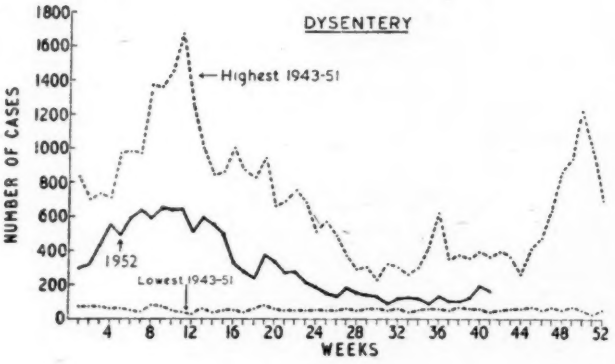
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1943–51 are shown thus - - - - - -, the figures for 1952 thus ————. Except for the curves showing notifications in 1952, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending October 18

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,760, whooping-cough 1,074, diphtheria 29, measles 7,785, acute poliomyelitis 119, dysentery 181, paratyphoid fever 15, and typhoid fever 6.

Road Accidents in September

Casualties on the roads of Great Britain in September are provisionally estimated at 18,074. The number of deaths reported is 411, and the number of seriously injured 4,379. These figures may be slightly increased when final returns are received. Even so, it is expected that they will be well below the total for September, 1951, when there were 19,810 casualties, including 438 killed and 4,753 seriously injured.

Medical News

Society of Medical Officers of Health.—The principal guest at the annual dinner of the Society of Medical Officers of Health on October 23 was the Rt. Hon. Iain Macleod, M.P., Minister of Health. In proposing the health of the Society, Mr. Macleod confessed that he was not happy in his mind concerning the relationship of local authorities to the health services. There were many problems not only unsolved but as yet completely untouched. One of them was whether local authorities should or should not have more voice in the appointments that were made to the hospitals within their area; another was whether medical officers of health stood in the right relationship to the healing profession in general and to the hospitals. But it was unlikely that these and other problems would begin to be solved until there was a rational solution of local authority administration. Dr. Andrew Topping, president of the Society, said in response that, while many might agree that the taking away of hospital functions from the medical officers of health was perhaps not a bad thing, local authorities had never received adequate credit for what they did in the development of hospitals in the period between the passing of the Local Government Act, 1929, and the National Health Service Act, 1946. He was still convinced that the White Paper produced by Mr. Willink was a better scheme than the one they had subsequently to adopt. Dr. Topping then criticized what he called "the stranglehold of consultants." Because a man had decided that he did not want to do general medicine, feeling that he had not the right philosophical or psychological approach, and decided instead to be an expert on allergy or anaesthetics, was it any reason why he should be looked upon as being on an entirely different and superior plane? The natural result was that the public said of a practitioner that he was an ordinary doctor and could not be very good, otherwise he would be in Harley Street. They had to improve the status of the general practitioner, whose services could be used much more in the hospitals. The toast of "The Guests" was proposed by Dr. C. F. White, Medical Officer of Health, City of London, and responded to by Mr. George North, Registrar-General, and by Dr. G. S. Wilson, Director of the Public Health Laboratory Service.

Memorandum on Immunological Procedures.—The War Office has issued a small pamphlet on immunization which will be appreciated by many besides Service medical officers. It is called "Memorandum on Immunological Procedures which Service Personnel and their Families may Need at Home and Abroad" (H.M.S.O., price 2s.). In addition to sections on inoculation technique, the storage of vaccines, and serum reactions, detailed advice is given about immunization against the enteric fevers, tetanus, gas gangrene, diphtheria, tuberculosis, cholera, plague, typhus, smallpox, yellow fever, and rabies.

Birth Control in India.—A field trial of the "safe period" as a means of contraception will soon be started in India. The professor of statistics of Stockholm University, Professor Sten Wahlund, has just left for India to advise the Government on the investigation. Several thousand families in the State of Mysore are to be given detailed instruction about the "safe period," and their birth rate will be compared with that of an uninstructed control group. Preliminary results are expected about 18 months after the start of the trial.

Unit for Barbiturate Poisoning.—At its meeting on October 22 the North-east Metropolitan Regional Hospital Board gave its blessing to the establishment of a 10-bed unit at Oldchurch Hospital, Romford, for the treatment of cases of barbiturate poisoning. It is estimated that the unit could deal with about 500 cases a year, so that admissions will have to be from a wide area to keep it busy. In presenting the case for the new unit Dr. James Graham, the Board's senior administrative medical officer, said that between 1946 and 1949 there had been 884 deaths from barbiturate poisoning in England and Wales and that more recent figures were expected to show an increase.

Guinness Research Fellowships.—Oxford University has accepted a sum of £2,500 a year for seven years from Arthur Guinness, Son and Co. Ltd. to establish three research fellowships in microbiological biochemistry. Fellows must be British graduates with experience of research, and they will be expected to work in the department of biochemistry at Oxford. The fellowships will be tenable for three years in the first instance, and may be renewed for a further two years. The stipend is between £600 and £800 a year.

Leverhulme Research Fellowships.—Application is invited for fellowships and grants in aid of research intended for senior workers who are prevented by routine duties or pressure of other work from carrying out research. They are limited to British-born subjects normally resident in the United Kingdom. (In exceptional circumstances the trustees may waive the condition as to residence.) The trustees are also prepared to consider applications from groups of workers engaged upon co-operative programmes

of research, particularly if long-term. The duration of the awards will not normally extend over more than two years or less than three months, and the amount will depend on the nature of the research and the circumstances of the applicant. Forms of application may be obtained from the secretary, Leverhulme Research Fellowships, 3–5, Salisbury Square, London, E.C.4. Applications must be received on or before December 31. Awards will be announced in May and will date from September, 1953.

Emergency Bed Service: Applications and Admissions.—During the seven days ending October 27 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 1,060, of which 92.42% were admitted. This information will in future be published weekly in these columns. The applications include those from general practitioners and those from hospitals wanting to transfer patients from their casualty or out-patient departments. The gap between the number of applications and the number admitted is not composed entirely of cases that fail to be admitted. Some cases are withdrawn by the doctor or hospital while the E.B.S. is still working on the case, and some cases are of patients who refuse to go to hospital when a bed has been found or who die before admission.

International Course at Roehampton.—A two-weeks training course on the manufacture and fitting of artificial limbs and the rehabilitation of amputees is now being held at Queen Mary's Hospital, Roehampton. The course is sponsored by the World Veterans Federation and the International Society for the Welfare of Cripples. It is being attended by surgeons and technicians from Finland, Italy, Israel, Belgium, Holland, Yugoslavia, and Denmark.

Royal Academy of Medicine in Ireland.—The following officers have been elected for the coming session: *President*, Mr. T. O. Graham; *General Secretary*, Professor T. P. C. Kirkpatrick; *Secretary for Foreign Correspondence*, Mr. W. Doolin.

Sir Alexander Fleming was accorded two unusual honours while in Greece last week. At Athens he was made an associate member of the Academy of Athens; during the ceremony he was given a branch from the olive tree beneath which Plato is supposed to have taught. At Salonika the town council has decided to name a street after him.

Dr. H. V. Morgan, first assistant to the Medical Professorial Unit at St. Bartholomew's Hospital, has been appointed professor of medicine at Khartum. Dr. Morgan qualified in 1940, and has since held a British Postgraduate Federation travelling fellowship.

Dr. G. S. Wilson, director of the Public Health Laboratory Service, has been to Dubrovnik, Yugoslavia, where he presided at a World Health Organization conference on diphtheria and whooping-cough vaccines.

COMING EVENTS

Public Works and Municipal Services Congress.—During the progress of this Congress, on November 6 at 2.30 p.m. at Olympia, Lieutenant-Colonel E. F. W. Mackenzie, of the Metropolitan Water Board, will present a paper on "The Prevention of Dental Caries by the Administration of Fluorine in Public Water Supplies." Members of the B.M.A. will be welcome at this session; admission is by special ticket, for which application should be made to the secretary, British Waterworks Association, 34, Park Street, London, W.1.

Empire Rheumatism Council Week-end Course.—The Empire Rheumatism Council has arranged a week-end course of lecture-demonstrations on rheumatic disorders, at the Arthur Stanley Institute, Middlesex Hospital, Marylebone Road, London, N.W.1, on November 21 and 22, 1952. The speakers will include Professor R. E. Tunbridge, Dr. G. D. Kersley, Dr. A. C. Boyle, Mr. Norman Capener, Dr. H. J. Gibson, Dr. F. Dudley Hart, and Dr. H. F. West. The fee for the course is two guineas. Further information can be obtained from the General Secretary, Empire Rheumatism Council, Tavistock House North, Tavistock Square, London, W.C.1.

Research Defence Society Lecture.—The 21st Stephen Paget Memorial Lecture will be delivered to the Research Defence Society by Sir Howard Florey on November 20 in the physiology lecture theatre, University College, Gower Street, London, W.C.1, at 5.30 p.m. His subject will be "The Advance of Chemotherapy by Animal Experiment." The lecture will be followed by the annual general meeting of the society.

London Medical Exhibition.—The London Medical Exhibition will take place at the New Hall of the Royal Horticultural Society, Greycoat Street, London, S.W.1, from November 17 to 21. The exhibition will be opened by Sir Cecil Wakeley at 12 noon on November 17. The exhibition is to allow members of the medical profession to inspect new pharmaceutical products, surgical instruments, and hospital equipment. The public are not admitted, but doctors are welcome.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, November 3

●INSTITUTE OF CHILD HEALTH, Hospital for Sick Children, Great Ormond Street, London, W.C.—5.30 p.m., *"Animal Epidemiology"* by Professor N. J. Scorgie.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5 p.m., *"Streptomycin and Other Newer Antibiotics,"* by Mr. Arnold Sorsby.

SOCIETY OF APOTHECARIES OF LONDON, Black Friars Lane, Queen Victoria Street, E.C.—3.30 p.m., *"Surgery of Diseases of the Chest,"* by Mr. T. Holmes Sellors; 5 p.m., *"The Medical Aspect of Diseases of the Chest,"* by Sir Geoffrey Todd.

Tuesday, November 4

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, W.C., 5.30 p.m., *"Life at High Altitudes,"* by Sir Bryan Matthews, Sc.D., F.R.S.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—5.30 p.m., *"Genetics,"* by Dr. C. O. Carter.

SOCIETY OF APOTHECARIES OF LONDON, Black Friars Lane, Queen Victoria Street, E.C.—3.30 p.m., *"Changes in Obstetrics and Gynaecological Practice in the Last Fifty Years,"* by Sir William Gilliatt; 5 p.m., *"Pitfalls in Diagnosis of Coronary Thrombosis,"* by Dr. Kenneth Harris.

WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane, London, W.—5.30 p.m., neurological demonstration by Dr. C. Worster-Drought.

Wednesday, November 5

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—5.30 p.m., *"Epitheliomata,"* by Dr. J. O. Oliver.

●LONDON MARRIAGE GUIDANCE COUNCIL, 78, Duke Street, Grosvenor Square, W.—6.30 p.m., *"Homosexuality,"* by Dr. Clifford Allen.

MANCHESTER MEDICAL SOCIETY: SECTION OF MEDICINE.—4.30 p.m., *"Recent Advances in Diabetes,"* by Dr. W. G. Oakley.

MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 8.15 p.m., *"Management of Mitral Stenosis,"* by Professor W. M. Arnott and Mr. A. L. d'Abreu.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5.30 p.m., *"Differential Diagnosis of Headaches,"* by Mr. L. H. Savin.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—3.30 p.m., *"The Work of the World Influenza Centre"* (illustrated), by Dr. C. H. Andrewes, F.R.S.

SOCIETY OF APOTHECARIES OF LONDON, Black Friars Lane, Queen Victoria Street, E.C.—3.30 p.m., *"Some Medical Aspects of Hypertensive Disease,"* by Sir Horace Evans; 5 p.m., *"A Review of Surgical Management of Hypertension,"* by Mr. A. Dickson Wright.

SOCIETY OF PUBLIC ANALYSTS AND OTHER ANALYTICAL CHEMISTS.—At Chemical Society's rooms, Burlington House, Piccadilly, London, W., 7 p.m., *"The Bio-assay of Vitamins, with Special Reference to Microbiological Methods."* Papers by Mr. L. J. Harris, Sc.D., Mr. H. Pritchard, M.Sc., and Mr. E. C. Wood, Ph.D.

Thursday, November 6

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, W.C., 5.30 p.m., *"Physiological Effects of Gravity,"* by Group Captain W. K. Stewart, R.A.F.

FACULTY OF HOMOEOPATHY.—At Royal London Homoeopathic Hospital, Great Ormond Street, W.C., 5 p.m., *"The Place of Homoeopathy in Psychiatry,"* address by Dr. F. H. Bodman.

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY.—At Glasgow University Union, 7.30 p.m., *"Fallacies about the Prostate,"* by Mr. T. L. Chapman.

HONYMAN GILLESPIE LECTURE.—At University New Buildings (Anatomy Theatre), Teviot Place, Edinburgh, 5 p.m., *"Melanoma,"* by Mr. J. R. Cameron.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—5.30 p.m., *"Specific and Foreign Body Granulomas,"* by Dr. H. Haber.

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant.—8 p.m., ordinary meeting. *"Avoidable Stillbirths and Neonatal Deaths,"* by Mr. John Hamilton.

LONDON UNIVERSITY.—At Royal Society of Medicine, 1, Wimpole Street, W., 5 p.m., *"Clinical Aspects of Respiratory Air Currents,"* Semon Lecture by Professor Arthur W. Proetz (University of Washington).

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, London, S.W.—5 p.m., *"Changing Concepts of Health and Disease, with Particular Reference to 'Psychosomatic Medicine,'"* Bradshaw Lecture by Dr. R. B. Bomford.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—4.30 p.m., *"Random Reminiscences of Fifty Years,"* Frederic Hewitt Lecture by Dr. C. F. Hadfield.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5.30 p.m., *"Squint,"* by Miss J. M. Dollar.

ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION.—At Royal Society of Medicine, 1, Wimpole Street, London, W., 2.15 p.m., *"The Unwilling Patient,"* 27th Maudsley Lecture by Dr. W. Rees Thomas.

ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, 5 p.m., *"Cholesterol and Atherosclerosis,"* by Professor J. B. Duguid.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—5 p.m., lecture-demonstration in neurology by Dr. D. Williams.

SOCIETY OF APOTHECARIES OF LONDON, Black Friars Lane, Queen Victoria Street, E.C.—3.30 p.m., *"Medico-legal Hazards in General Practice,"* by Dr. Robert Forbes; 5 p.m., *"Present and Future Trends in General Practice,"* by Dr. R. Hale-White.

UNIVERSITY COLLEGE, Anatomy Theatre, Gower Street, London, W.C.—1.15 p.m., *"The Biology of Bubonic Plague,"* by Mr. R. B. Freeman.

Friday, November 7

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—5.30 p.m., *"Congenital and Developmental Abnormalities,"* clinical demonstration by Dr. H. J. Wallace.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5 p.m., *"The Diagnostic Value of X-rays in Ophthalmic Work,"* by Dr. J. Blewett.

ROYAL INSTITUTE OF PHILOSOPHY.—At University Hall, 14, Gordon Square, London, W.C., 5.15 p.m., *"Mind and Its Place in Nature,"* Manson Lecture by Dr. O. L. Zangwill.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—8 p.m., *"Some Contributions to Paediatrics by Members of the Royal Medical Society,"* by Mr. J. J. Mason Brown.

Saturday, November 8

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.—11.30 a.m., *"Olfaction,"* by Dr. Arthur W. Proetz (University of Washington).

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, Ducane Road, London, W., 12 noon, *"Uterine Rupture,"* Guest Lecture by Professor W. I. C. Morris.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brook.—On October 19, 1952, at St. Mary's Hospital, Kettering, Northants, to Alexis (formerly Ormrod), wife of Dr. Maurice Handford Brook, a son—Michael Brian Clothus.

Brown.—On October 24, 1952, at King's College Hospital, London, S.E., to Jean, wife of Dr. R. J. K. Brown, a son—Arthur Nicholas.

Davidson.—On October 6, 1952, at Nicosia, to Helen Audry, M.B., B.Ch. (formerly Lynas), wife of Malcolm Norman Davidson, Colonial Administrative Service, Cyprus, a daughter.

Edelman.—On October 19, 1952, at Hillingdon Hospital, Middlesex, to Jacqueline (formerly Heller), wife of Dr. Seymour Edelman, of 267, Church Road, Hayes, Middlesex, a son—Ian Philip.

Hamlett.—On October 13, 1952, at Skegness District Hospital, to Marjorie (formerly Taylor), wife of Dr. J. W. Hamlett, M.B., M.R.C.S., R.A.F., a son—Andrew John.

James.—On October 9, 1952, at Beechfield Nursing Home, South Croydon, Surrey, to Linda, wife of Dr. N. M. James, a daughter.

Rutter.—On September 13, 1952, to Mary (formerly Milton), wife of Dr. Frank W. E. Rutter, of Peterston-s-Ely, Glam, a daughter.

MARRIAGES

Kerr—Balchin.—On September 13, 1952, at Loose, Kent, Geoffrey Alan Kerr, M.R.C.S., L.R.C.P., L.D.S., to Betty Agnes Balchin, S.R.N.

Rutherfoord—Tomlinson.—On October 18, 1952, at Chiswick, London, W., Geoffrey Temple Rutherfoord, M.B., to Teresa Elizabeth Tomlinson.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Premature Induction of Labour in Haemolytic Disease of the Newborn

Q.—*Should labour be induced before term when an antenatal diagnosis of haemolytic disease of the newborn has been made?*

A.—All that can be said with certainty about premature induction of labour is that if it is practised as a routine in women whose serum contains anti-Rh it will increase infant mortality. There may be a case for performing premature induction of labour in women who have had previous stillbirths due to Rh incompatibility, although it has never been shown that this does in fact increase the survival rate. The best rule is: When in doubt do not induce labour prematurely.

Antenatal Diagnosis of Haemolytic Disease of the Newborn

Q.—*How much help will serology give in deciding whether an infant is likely to be affected by haemolytic disease? Is the severity of the disease related to the agglutinin titre, and, if so, what levels should cause alarm?*

A.—The finding of Rh antibody in the serum of an Rh-negative woman who is not pregnant or who has not advanced beyond the twelfth week of pregnancy indicates either that she has previously given birth to an Rh-positive infant or that she has previously received a transfusion or injection of Rh-positive blood. Once Rh antibody has been formed the subject continues to produce it; thus if a woman has once formed Rh antibody it may be found in her serum during a subsequent pregnancy even though she is then carrying an Rh-negative foetus.

When Rh antibody is absent from a woman's serum during the first three or four months of pregnancy but makes its appearance later it may be assumed that the infant *in utero* is Rh-positive and will be affected with haemolytic disease of the newborn to a greater or lesser extent. If antibody appears for the first time during the last few weeks of a pregnancy it is likely that the infant will be extremely mildly affected.

Two forms of Rh antibody may be recognized in the serum: namely, saline agglutinin—a form capable of agglutinating Rh-positive cells suspended in saline; and incomplete antibody—a form which agglutinates Rh-positive cells only when they are suspended in certain colloid media. Only the incomplete antibody crosses the placenta; thus a report that a serum contains incomplete antibody has a more serious significance than a report of the presence of saline agglutinin. However, it has to be remembered that saline agglutinin is almost invariably accompanied by a certain amount of incomplete antibody, so that a report that saline agglutinin is present does not imply that the infant will be unaffected. On the whole, the higher the titre of incomplete antibody, the worse the prognosis; however, individual exceptions are not uncommon and infants with hydrops foetalis may be born to women whose serum has an anti-Rh titre of only 1 in 8. In view of the frequency of exceptions it is unwise to be much influenced by the result of anti-Rh titrations. The safest plan is to deliver all women whose serum contains Rh antibody in a hospital where there are facilities for performing exchange transfusion, since there is now decisive evidence that this treatment gives the infant its best chance of recovery.

Angular Stomatitis

Q.—*Can you describe the aetiology and treatment of a recurrent painful fissuring of the angles of the mouth? The condition has persisted for four months and does not respond to antibiotics, emollient creams, or vitamin-B therapy. The patient is a married woman of 32, otherwise healthy. The fissure occasionally heals, when the skin at the red margin of the lip has an unhealthy pallor, but after a few days a crack appears, which gradually deepens. This does not normally extend beyond the red margin. Is the condition infectious, and may it be fungal in origin?*

A.—In the absence of nutritional disturbances and of local infective causes, which appear to have been considered, a common cause of angular stomatitis is faulty alignment of the teeth and jaws. This faulty "bite" may occur with both natural and artificial teeth, and can usually be corrected by dental attention. The maladjustment of the teeth causes a folding of the skin at the angles of the mouth, with consequent maceration and infection. Some individuals, and particularly seborrhoeic subjects, are more prone to trouble from this source. It is important to exclude any chronic infection in the nose or throat, accessory sinuses, or jaws.

With artificial dentures, an allergic sensitiveness to the material of the denture may determine an angular stomatitis without necessarily producing inflammation inside the mouth. This is particularly likely to happen if the dentures are not removed at night. Less commonly, sensitiveness to lipstick may also be responsible.

A gentian violet cream at night and fractional doses of *x* rays are useful local measures, but cure depends upon removal of the cause.

Temperature and Humidity of Operating Theatres

Q.—*What is the optimum temperature and humidity for an operating theatre?*

A.—I am not aware of any physiological investigation into the optimum temperature and humidity for an operating theatre, but experience in the dressing station of the Burns Unit of the Birmingham Accident Hospital suggests that a temperature of 72° F. (22.2° C.) and a relative humidity of about 50 to 55 is satisfactory both for an exposed patient and for the staff. For a very sick patient who has to be exposed for a long time the temperature is sometimes increased to 74° F. (23.3° C.).

The "Dumping Syndrome"

Q.—*What precisely is meant by the term "dumping syndrome" after partial gastrectomy? Are there any specific signs and symptoms by which it is recognized, and are the x-ray findings characteristic of the condition?*

A.—The term "dumping syndrome" is better called "post-gastrectomy syndrome." It covers a number of quite different phenomena. There are three main groups of these: vaso-vagal attacks, hypoglycaemic attacks, and "neurotic" attacks.

Vaso-vagal attacks come on a few minutes after the ingestion of food and are characterized by faintness, sweating, pallor, a feeling of warmth, nausea, palpitations, and a sense of epigastric fullness. These are probably due to over-distension of a small stomach remnant and the drag of this and the anastomotic loop on the gastro-oesophageal junction, the stimulus being conveyed by the splanchnic nerves. Some distension of the proximal loop with bile may be a subsidiary factor. Hypoglycaemic attacks occur two to three hours after the taking of a meal and are due to the rapid emptying of the stomach remnant into the jejunum of unacidified and undigested food. The third group is characterized by vague and indeterminate symptoms with no time relation to a meal. Patients with these symptoms are those who have made a habit of "enjoying" their stomach symptoms, and who will continue to indulge that habit irrespective of treatment.

X-ray findings are of little value in the elucidation of post-gastrectomy symptoms, apart from confirming a small gastric remnant.

Order of Depletion in Starvation

Q.—*In starvation, in what order are the tissues depleted? How early is nervous tissue affected?*

A.—It is generally accepted, on the basis of clinical observations and animal experiments, that the adipose tissues are first expended, and that reductions then occur in the weights of the muscles, glandular organs, and blood. The heart, lungs, and nervous tissues are more resistant, and the skeleton and eyes least affected of all. Thus in early work quoted by Lusk (*The Science of Nutrition*, 4th ed., 1928; W. B. Saunders, Philadelphia) the percentage losses found in the various organs of a dog after a fast of 24 days were as follows: pancreas 62, spleen 57, kidneys 55, liver 50, genitals 49, blood 48, muscles 42, stomach and intestines 32, lungs 29, skin 28, brain and cord 22, heart 16, skeleton 5, and eyes 3. During the second world war, however, the relatively high resisting powers of the nervous tissues did not prevent the frequent appearance of nervous symptoms, such as "burning feet," in prisoners in Oriental internment camps who had to subsist for long periods on grossly inadequate diets.

Two Unsuccessful Pregnancies

Q.—*What is the chance of a young woman having a normal baby after two unsuccessful pregnancies? The first ended in an unexplained abortion at the third month, and the second in an anencephalic monster. She is rhesus negative and no abnormal antibody has been detected; Kahn negative. Are any special investigations indicated?*

A.—The first pregnancy often ends in abortion for no obvious reason, and such an occurrence is usually of little significance in relation to the future. The birth of an anencephalic monster in the second pregnancy in this case, however, raises the possibility that the first foetus may also have been malformed in some way. After one anencephalic monster the risk of a couple having a second malformed child is generally placed at 1 in 40. If, however, it is assumed that both the foetuses in this case were abnormal, the risk will be further increased, but not so much that it would be right to advise the couple against further child-bearing. Nothing can be done to reduce the risk, and no further investigation is likely to be profitable at this stage.

NOTES AND COMMENTS

Corrections

We regret that Professor Harold Dew's name was misspelt in a recent note on the Sims Commonwealth Professors (*Journal*, October 18, p. 887).

The visual aid mentioned in the *Journal* of October 4 (p. 787) consists in a set of charts prepared from the filmstrips described in our paragraph, not of the filmstrips themselves. The cost of hiring the charts is one guinea a week.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London*. ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
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